New Microbes and New Infections 55 (2023) 101187

Contents lists available at ScienceDirect

New Microbes and New Infections

journal homepage: www.journals.elsevier.com/new-microbes-and-new-infections

Letter to the Editor

Vaccination gaps and resurgence of diphtheria in Nigeria: An outbreak simmering for a catastrophe

To the Editor,

Diphtheria is a highly contagious and potentially fatal infection caused by *Corynebacterium diphtheriae* and occasionally by *C. ulcerans* and *C. pseudotuberculosis* strains [1]. The bacterium primarily causes an acute respiratory infection, forming a firmly adherent throat pseudomembrane in the throat, pharynx, and tonsils, causing a swollen neck ("bull neck"). The pathogenesis of *C. diphtheriae* is based on its ability to produce diphtheria toxin that can cause extensive damage to the organs and may lead to death if untreated. The toxigenic effects of *C. diphtheriae* are mainly due to a lysogenic bacteriophage carrying the diphtheria toxin gene (tox) gene that affects protein synthesis. Therefore, the toxin causes inflammation of the upper respiratory tract mucosal surfaces, nerves and heart lesions, leading to symptoms such as sore throat, fever, breathing difficulties, heart rhythm problems, and rarely membranous pharyngitis. Systemic infections such as myocarditis and neuropathy are also associated with diphtheria toxin, thus increasing morbidity and mortality [2]. Transmission of diphtheria is common through inhalation of airborne droplets, sneezing, coughing, or handling contaminated personal items (https://www.cdc.gov/vaccines/pubs/surv-manual/).

Diphtheria is a treatable disease with timely administration of antimicrobial therapy and tetanus toxoids/diphtheria antitoxin (DTaP). On the other hand, effective vaccines are also available that have led to a decline in active cases globally. Worldwide, the case-fatality ratio for diphtheria has been estimated to be between 5 and 10% in high vaccination coverage areas. However, in low-income countries, especially in Asia and Africa, low vaccination uptake and coverage and poor sanitation conditions have led to the re-emergence of diphtheria, with thousands of diphtheria cases and outbreaks reported annually. In such regions, the case-fatality ratio in children under five and adults above 40 years has been approximated to be as high as 20% (https://www.cdc.gov/vaccines/pubs/pinkbook/index.html).

In 2023, the World Health Organization (WHO) (https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON452) reported an alarming number of cases in Nigeria with overall risk of diphtheria assessed as high at the national level. Since the beginning of 2023, out of 1439 suspected cases, 557 cases (39%) have been confirmed, with 73 deaths among these cases, raising the case fatality ratio to 13% in this region. WHO has identified 21 of the 36 states and the Federal Capital Territory as severely affected by the diphtheria outbreak (Fig. 1). This ongoing outbreak is mainly observed in children aged 2 to 14, particularly in the Kano state. According to the Nigeria Centre for Disease Control (NCDC), only a fraction of the cases were fully vaccinated with the diphtheria-tetanus-pertussis (DTP3) vaccine, indicating the considerable role of the vaccine in control of this disease (https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON452).

According to WHO and NCDC, several factors are associated with the outbreak of diphtheria cases in Nigeria, including suboptimal vaccination coverage, especially for the diphtheria toxoid-containing vaccine third dose, notably in areas controlled by non-state armed groups; overstretched resources with a limited supply of diphtheria antitoxin (DAT) that affects the availability of the required doses in a timely manner; poor sanitary conditions and access to proper healthcare; limited clinical and epidemiological studies to quickly identify and treat affected individuals; and, paucity of public health measures to prevent and contain the spread of this disease [1].

These factors are based on the epidemiological history of diphtheria assessed and reported by a number of experts. Data from 2015 to 2023 declared by the NCDC indicates a history of underrepresentation of data and considerable gaps in vaccination coverage, leading to such high cases and outbreaks in Nigeria [3]. In lieu of this perspective, if we look at the reported data, a stark contrast is observed every year. For example, in 2023, a massive outbreak of 553 confirmed cases and 73 deaths has been reported. It is believed to have started in late December 2022 in Kano State, with many patients also reported from Lagos, Osun, and Yobe States.

On the other hand, in 2021, only 160 cases were reported, with most of the cases reported in the northern part of the country, with Kano, Bauchi, and Yobe States having the highest number of cases. Similarly, in 2020 and 2019, only 245 and 157 cases were reported from 25 States of the country, with the highest number of cases reported in Katsina, Zamfara and Kano States. In contrast, in 2018, a large diphtheria outbreak was reported, with 176 confirmed cases and 22 fatalities reported mainly in four states: Adamawa, Bauchi, Borno, and Kano [3]. Similar to these contrasting reports on number of cases, the same pattern is observed in case fatality rates (CFR) reported by NCDC with significant variations. In 2020 no case fatality was reported, while in 2021, only 5% CFR was reported. In 2023, WHO reported a case fatality rate of 13% in Nigeria, which is high compared to the data from previous years [3].

The sharp contrast of CFRs indicates a possible underrepresentation of data in previous years, possibly due to political unrest, constrained resources for data collection, and COVID-19-associated disruption, among others. On the other hand, Nigeria's primary age group trend from 2020 to 2023 was observed to be highest in children under 15 years of age, with the most affected age group being children between 5 and 14 years [3]. Low vaccine coverage has pushed these vulnerable groups towards the risk of diphtheria-related morbidity and mortality. Accordingly, an efficient vaccine coverage program with trained healthcare staff could have prevented these vulnerable groups from diphtheria risk. Similarly, the availability of timely antitoxins and antimicrobial medications could have prevented most of the mortalities. Unfortunately, political unrest, constrained resources, poor healthcare

https://doi.org/10.1016/j.nmni.2023.101187
Received 1 October 2023; Received in revised form 6 October 2023; Accepted 9 October 2023
Available online 10 October 2023
2052-2975/© 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

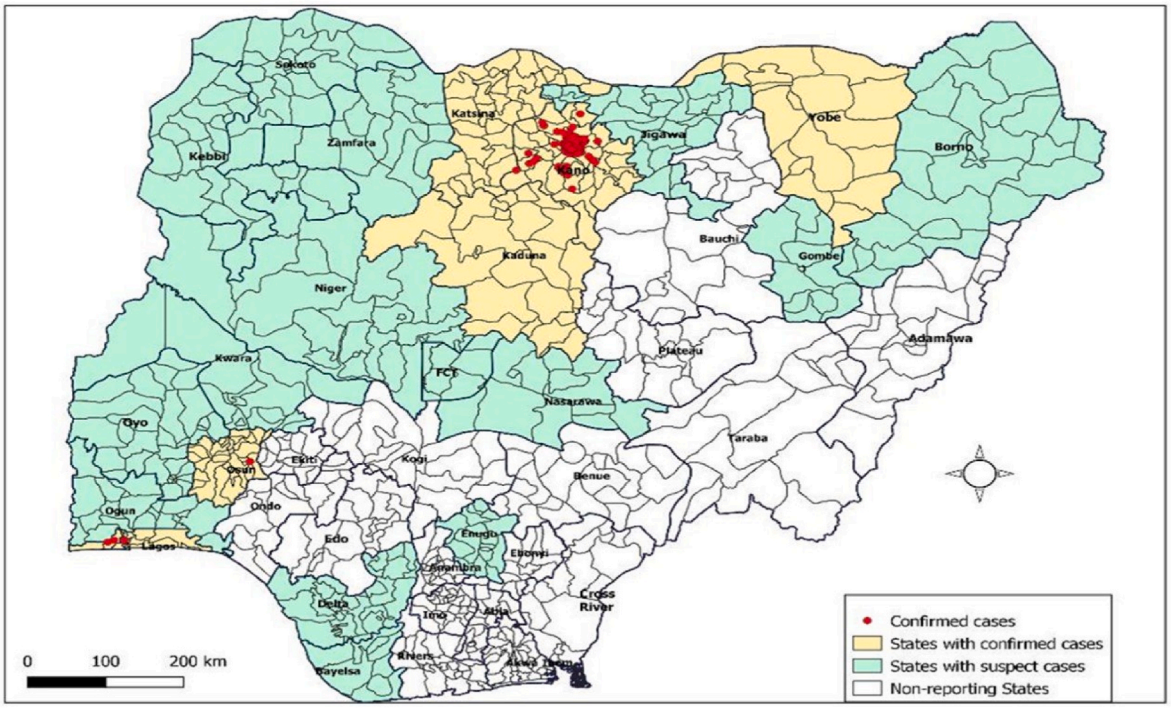


Fig. 1. Distribution of Diphtheria cases by state in Nigeria from epidemiological week 19, 2022, to epidemiological week 14, 2023 (WHO) (https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON452).

availability with clinicians having limited experience of managing the disease and underrepresentation of cases may have pushed these vulnerable groups towards this highly morbid and fatal consequence. Several studies have also reported that the resurgence and re-emergence of diphtheria is mainly due to significant variations in DPT3 immunization coverage across Nigerian states. An approximate suboptimal coverage of <20%–80% with an overall coverage of 56% indicates a huge gap in healthcare services leading to high diphtheria cases especially in children under-five years of age (https://immunizationdata.who.int/pages/coverage/dtp.html). The low vaccine coverage is also associated with social factors including a) lack of maternal education about DPT vaccine; b) misconceptions or suspicious beliefs including misinformation and mistrust in vaccines; c) perceived harm due to reported adverse events following immunization; d) household decision-making dynamics with uneducated males lacking the awareness and thus making it difficult for children to receive vaccinations; e) religious beliefs that hinder vaccine coverage; f) poor proximity to health facilities; g) shortage of healthcare workers enabling vaccine access; h) COVID-19 restrictions and lockdowns resulting in decreased vaccine uptake, and discontinuation of mobile vaccination campaigns that targeted hard-to-reach communities. Considering these factors, significant changes in the healthcare infrastructure, access and public awareness of vaccinations could be essential in managing this outbreak in Nigeria.

As of 2023, a considerable outbreak is ongoing, and Nigeria is on the verge of a catastrophic disaster. Now is the time to make changes and allow the NCDC, Non-government organizations (NGOs) and government healthcare systems to work together to prevent further outbreaks. The country is already under several public health emergencies, such as Lassa fever, cholera, mpox, meningitis, and the outbreak of diphtheria could add another layer of difficulty to this situation. On the other hand, a humanitarian emergency in the northeast of the country with political unrest has affected healthcare coverage with inadequate expenditure and funding for immunization programs, disease surveillance and response, leading to the limited supply of diphtheria antitoxin (DAT), and inadequate access to health care for the poverty-stricken. The situation in Nigeria is hazardous and could trigger an outbreak bigger than the country can handle. Therefore, future recommendations to control and manage this alarming situation in Nigeria include increasing funding for immunization programs; building the infrastructure for disease surveillance and response with efficient distribution of DAT to the affected states; increasing access to health care; educating with public awareness programs; increased monitoring of diphtheria surveillance and response activities with Rapid Response Teams by NCDC; and, sensitization/training of clinical and surveillance officers. Between 30 June and 31 August 2023, Nigeria recorded increased confirmed diphtheria cases. From 30 June to 31 August 2023, 5898 suspected cases were reported from 59 LGAs in 11 states nationwide. The majority (99.4%) of suspected cases were reported from Kano (1816), Katsina (234), Yobe (158), Bauchi (79), Kaduna (45) and Borno (33).

It is imperative that with the implementation of these fundamental recommendations, the outbreaks can be managed for this easy-to-treat disease. Support from humanitarian groups and various limited-resource countries could mitigate this alarming situation and help vulnerable groups [4]. The WHO and NCDC should aim to work together to manage this simmering catastrophe that can end in disaster for this resource-constrained, politically unstable country and could push vulnerable children and young adults to the verge of a highly morbid and fatal disease that can be easily controlled through effective vaccination and healthcare programs [5].

Sources of funding

No financial support was available for this study.

Author contribution

AR and SH: designed the study; AR: made the first draft; AR, JJMI, AJRM and SH: updated the manuscript; SH: reviewed the final draft. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Declaration of competing interest

The authors do not have conflicts of interest.

References

[1] Aborode AT, Ajagbe AO, Adewunmi RO, Fasawe AS. Resurgence of diphtheria outbreak in Nigeria. New Microbes New Infect 2023;53:101125.
[2] Holmes RK. Biology and molecular epidemiology of diphtheria toxin and the tox gene. J Infect Dis 2000;181(Suppl 1):S156–67.
[3] Medugu N, Musa-Booth T, Adegboro B, Onipede A, Babazhitsu M, Amaza R. A review of the current diphtheria outbreaks. Afr J Clin Exp Microbiol 2023;24:120–9.
[4] Mezones-Holguin E, Al-Kassab-Córdova A, Maguiña JL, Rodriguez-Morales AJ. Vaccination coverage and preventable diseases in Peru: reflections on the first diphtheria case in two decades during the midst of COVID-19 pandemic. Trav Med Infect Dis 2021;40:101956.
[5] Adegboye OA, Alele FO, Pak A, Castellanos ME, Abdullahi MAS, Okeke MI, et al. A resurgence and re-emergence of diphtheria in Nigeria, 2023. Ther Adv Infect Dis 2023;10:20499361231161936.

Afsheen Raza
Department of Biomedical Sciences, College of Health Sciences, Abu Dhabi University, Abu Dhabi, 59911, United Arab Emirates
E-mail address: raza.afsheen@adu.ac.ae.

Juan J. Montenegro-Idrogo
Master of Clinical Epidemiology and Biostatistics, Universidad Científica del Sur, Lima, Peru
Infectious and Tropical Diseases Service, Hospital Nacional Dos de Mayo, Lima, 15072, Peru
E-mail address: jmontenegroi@cientifica.edu.pe.

Alfonso J. Rodriguez-Morales*
Master of Clinical Epidemiology and Biostatistics, Universidad Científica del Sur, Lima, Peru
Gilbert and Rose-Marie Chagoury School of Medicine, Lebanese American University, Beirut, 11022801, Lebanon
Grupo de Investigación Biomedicina, Faculty of Medicine, Fundación Universitaria Autónoma de las Américas-Institución Universitaria Visión de las Américas, Pereira, 660003, Risaralda, Colombia

Shafiul Haque**
Research and Scientific Studies Unit, College of Nursing and Allied Health Sciences, Jazan University, Jazan, 45142, Saudi Arabia
Gilbert and Rose-Marie Chagoury School of Medicine, Lebanese American University, Beirut, 11022801, Lebanon
Centre of Medical and Bio-Allied Health Sciences Research, Ajman University, Ajman, 13306, United Arab Emirates

* Corresponding author.

** Corresponding author.
E-mail addresses: arodriguezmo@cientifica.edu.pe, alfonso.rodriguez@uam.edu.co (A.J. Rodriguez-Morales).
E-mail address: shafiul.haque@hotmail.com (S. Haque).