RISK ASSESSMENT AND MANAGEMENT OF DIPHTHERIA: STRATEGIES FOR PREVENTION AND CONTROL

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ABSTRACT
Background: Diphtheria, caused by *Corynebacterium diphtheriae*, poses a persistent global public health challenge despite vaccination efforts. This review aims to provide an overview of diphtheria, risk assessment, management strategies, and challenges in surveillance.
Methods: The review analyzed literature on diphtheria epidemiology, risk assessment, and management strategies, drawing insights from studies and reports on outbreaks, vaccination campaigns, and surveillance systems. Data from recent occurrences in Nigeria were analyzed to demonstrate the relevance of immunization and early detection in diphtheria management.
Results: Outbreaks in Nigeria highlight the critical role of immunization, with limited coverage contributing to recent occurrences. Prompt diagnosis and treatment with antibiotics and antitoxins are essential for managing diphtheria cases. Surveillance systems encounter challenges such as insufficient data collection and lack of centralized reporting, hindering effective control efforts.
Conclusion: Proactive approaches, including vaccination, hygiene promotion, and community engagement are crucial for preventing diphtheria spread and reducing its global burden. This review emphasizes the need for coordinated efforts to strengthen surveillance systems and improve vaccination coverage to control diphtheria transmission effectively.
Keywords: Immunization, Diphtheria, Toxin, Pseudo-membrane, Antimicrobial

INTRODUCTION
Diphtheria, an infectious disease caused by the bacterium *Corynebacterium diphtheriae*, poses a significant threat to public health worldwide. Historically, diphtheria was a major cause of morbidity and mortality, particularly among children, before the advent of widespread vaccination. Despite considerable progress in reducing its incidence through vaccination programs, diphtheria remains a concern, especially in regions with inadequate healthcare infrastructure and low vaccination coverage (Harapan *et al*., 2019; CDCP, 2024).
Diphtheria is characterized by the production of a potent exotoxin by *Corynebacterium diphtheriae*, leading to the formation of a thick, grayish membrane in the throat and upper respiratory tract. This toxin can cause local tissue damage and systemic effects, including myocarditis, neuropathy, and respiratory compromise. While respiratory diphtheria is the most common form of the disease, cutaneous and other less common manifestations can also occur (WHO, 2017).
Effective risk assessment and management are critical components of diphtheria prevention and control strategies. By identifying populations and settings at increased risk of diphtheria transmission,

as well as environmental and socioeconomic factors contributing to the disease spread, healthcare authorities can implement targeted interventions to mitigate the impact of the disease. Risk assessment informs vaccination strategies, surveillance systems, and public health interventions aimed at reducing diphtheria incidence and preventing outbreaks (Anthony *et al*., 2022; NCDC, 2024).

This presentation aims to give a thorough understanding of diphtheria, risk assessment, management techniques, and surveillance issues. The presentation will begin by elucidating the epidemiology and burden of diphtheria, highlighting global trends and regional disparities in disease incidence. Subsequently, the pathogenesis and clinical manifestations of diphtheria will be discussed to provide insights into disease mechanisms and presentation. The importance of risk assessment and management will be emphasized, underscoring the need for proactive measures to address diphtheria risk factors and enhance disease surveillance. Finally, the presentation will outline key strategies for diphtheria prevention and control, including vaccination programs, public awareness campaigns, and effective case management protocols.

BACKGROUND

Diphtheria, caused by toxin-producing strains of *Corynebacterium diphtheriae*, is a highly contagious but preventable communicable disease. While the bacterium primarily targets the pharynx, tonsils, and nose, its toxin can potentially harm vital organs like the heart, kidneys, and nervous system. The global case-fatality rate ranges from 5% to 10%, with a higher incidence (around 20%) observed in children under five and the elderly (Harapan *et al*., 2019). Despite successful elimination efforts in many countries, diphtheria is experiencing a resurgence, notably in the Republic of Indonesia, Southeast Asia's most populous nation. The bacterium's estimated basic proliferation number ranges from 1.7 to 4.3. Diphtheria, if identified at an early stage, can be controlled. However, if left untreated and unvaccinated, it can result in serious complications such as respiratory failure, cardiac problems, and a high rate of death (28.8-29.2%) (Acosta *et al*., 2021).

Abdulrasheed *et al*. (2022) reported that the Nigeria Centre for Disease Control (NCDC) was notified on December 1, 2022, about potential diphtheria outbreaks in Lagos and Kano, two of Nigeria's most populous states with a combined population exceeding 30 million. The director general of NCDC confirmed the outbreaks in Lagos and Kano through an advisory on January 20, 2023, and emphasized monitoring developments in Yobe and Osun, two additional states (Harapan *et al*., 2019; NCDC, 2023). As of February 3, 2023, the ongoing outbreak in Nigeria has resulted in 216 confirmed cases and 40 deaths, representing an 18.5% case fatality rate. Notably, Kano State has been significantly affected, accounting for 97.7% of cases, with children between 2- and 14-year-old constituting 85.2% of the affected population. Surprisingly, only a small percentage (12.5%) of the confirmed cases had received all three doses of the tetanus-diphtheria (TD3) vaccination (NCDC, 2023). This remains a public health concern in low-income nations, especially where vaccination rates are low, and sanitation conditions are substandard (CDC, 2020). Oleribe *et al*. (2017) asserted that cultural demographics, socioeconomic disparities and other factors, which will be explored further in this review, contribute to the decline in vaccination uptake in these rural areas. Despite the presence of a reliable vaccination, many impoverished nations continue to grapple with the public health challenge of tetanus (Orimadegun *et al*., 2014). Tetanus, caused by *Clostridium tetani,* is an acute, infectious, non-communicable disease with a high fatality rate. In 2013, according to World Health Organization data, 49,000 infants worldwide succumbed to this illness. The United Nations International Children's Emergency Fund (UNICEF) reported that one baby dies from tetanus every eleven minutes, translating to approximately 134 infants per day (UNICEF, 2021)

Globally, vaccine-preventable diseases stand as the leading cause of childhood morbidity and mortality, contributing to approximately 3 million deaths annually, predominantly in Asia and Africa (Galadima *et al.,* 2021). In Nigeria, about 50% of children lack the full three doses of the tetanus and diphtheria vaccine (TD+), a figure significantly below the WHO target of 90% coverage (Galadima *et al.,* 2021), as highlighted by Obanewa and Newell, (2020). Awosan *et al*. (2018) emphasize the danger of missing a dose or not receiving the TD+, citing a mortality rate of approximately 185 per 1000 under-five children. Manifesting symptoms encompass life-threatening coughs, neonatal, along with other lethal manifestations.

EPIDEMIOLOGY AND BURDEN OF DIPHTHERIA

Diphtheria, a bacterial infection caused by *Corynebacterium diphtheriae*, continues to pose a significant public health challenge globally, despite the availability of effective vaccines. The epidemiology and burden of diphtheria vary across different regions, with disparities in disease incidence, vaccination coverage, and healthcare infrastructure (CDCP, 2016).

Diphtheria in Nigeria

In Nigeria, diphtheria remains a concern, particularly in areas with limited access to healthcare services and low vaccination coverage. By October 5, 2023, the Federal Republic of Nigeria has experienced a substantial increase in diphtheria infections, with 13,145 reported cases and 493 deaths (NCDCP, 2023; Olulaja *et al*., 2023). The outbreak has been documented in eight Federal States, with Kano State seeing the most severe impact as a result of inadequate vaccination coverage for the pentavalent vaccine. While comprehensive epidemiological data on diphtheria are limited, sporadic outbreaks of the disease have been reported in various parts of the country (Figure 1). Factors contributing to the persistence of diphtheria in Nigeria include inadequate vaccination programs, poor sanitation and challenges in disease surveillance and reporting (NCDC, 2023).

Diphtheria in Africa

Diphtheria is endemic in several countries across Africa, where it disproportionately affects children and contributes to significant morbidity and mortality. Africa is currently facing repeated occurrences of infectious disease outbreaks, with diphtheria resurfacing in four African Union Member States: Algeria, Guinea, Niger, and Nigeria. As of October 9, 2023, a total of 14,587 cases have been documented in these Member States, with a case fatality rate of 4.1%. Nigeria alone is responsible for more than 90% of these cases (Rintani *et al*., 2018). The Republic of Niger officially announced the occurrence of the outbreak on August 17, 2023. In nine different areas, there were 865 confirmed cases and 37 fatalities; the majority of them occurred in the province of Matameye, which borders Nigeria. Guinea has reported a total of 497 cases, consisting of 14 confirmed cases and 483 suspected cases, along with 58 deaths. These cases are mainly concentrated in the Kankan region. Algeria has documented a total of 80 instances and 10 fatalities in the city of Tamanrasset, located in the southern region of the country. These cases have specifically impacted individuals from other countries who have not received any prior vaccinations (Ibrahim *et al*., 2022; Joel, 2023)

More than 65% of the documented diphtheria cases in Africa do not have a record of receiving vaccinations, and more than 60% of these cases include individuals who are under the age of 15. Women account for almost 62% of the recorded cases, and there have been a small number of instances documented among babies (Joel, 2023). Inadequate healthcare infrastructure, limited access to vaccines, and socioeconomic disparities exacerbate the burden of diphtheria in many African countries. Outbreaks of the disease are often associated with overcrowded living conditions, poor hygienic practices, and barriers to healthcare access (CDCP, 2024).

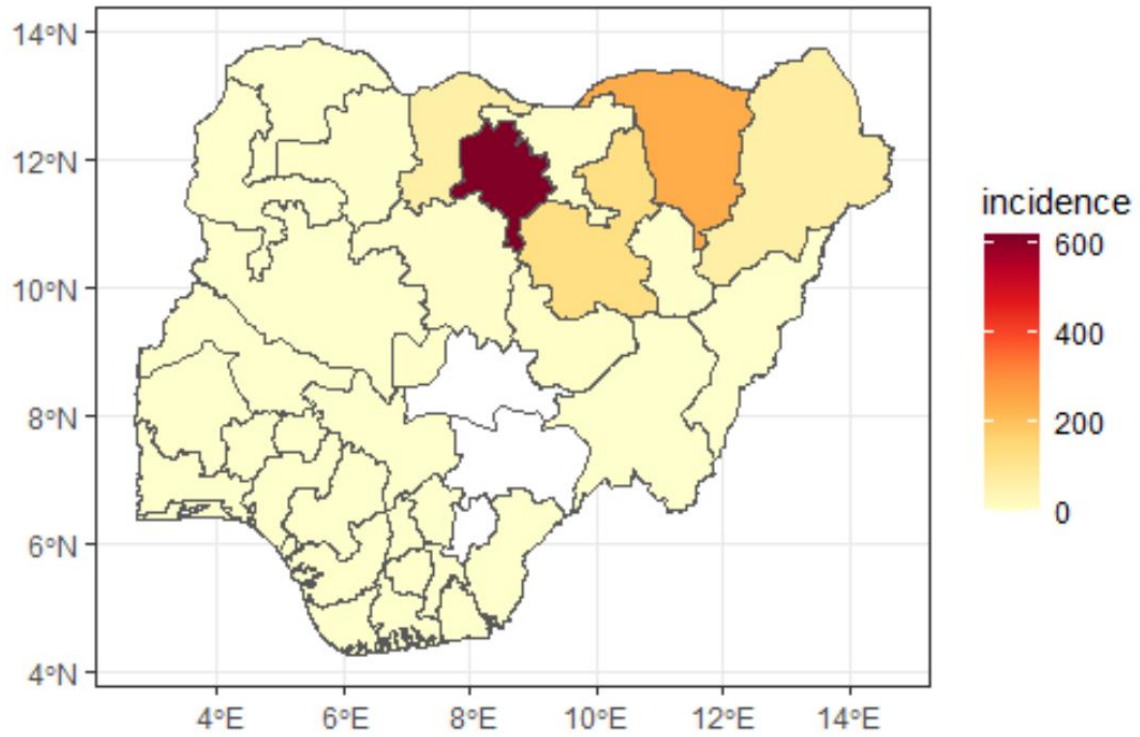

Figure 1: Incidence (per million population) of confirmed diphtheria cases in Nigeria by State, epi-week 19 2022 - epi-Week 51 2023 (NCDC, 2023)

Global Burden of Diphtheria

Globally, diphtheria incidence has declined substantially over the past century, largely due to the widespread use of diphtheria vaccines. However, the disease persists in certain regions, particularly in low- and middle-income countries with suboptimal vaccination coverage. According to the World Health Organization (WHO), an estimated 5,000 to 10,000 cases of diphtheria are reported annually worldwide, with the actual burden likely underestimated due to underreporting and gaps in surveillance systems (WHO, 2017).

Pathogenesis and Clinical Manifestations of Diphtheria

The bacteria *C. diphtheriae*, which causes diphtheria, is characterized by the production of a potent exotoxin known as diphtheria toxin. The pathogenesis of diphtheria involves toxin-mediated tissue damage and systemic effects, leading to a range of clinical manifestations (Harapan *et al*., 2019; CDCP, 2024).

Toxin Production

The hallmark of diphtheria pathogenesis is the production of diphtheria toxin by *Corynebacterium diphtheriae*. The diphtheria toxin is encoded by a bacteriophage and is released by toxigenic strains of *C. diphtheriae*. The toxin is an AB-type exotoxin, consisting of two subunits: an enzymatically active A subunit and a cell-binding B subunit. The B subunit facilitates binding of the toxin to host cells, while the A subunit enters the cell and inhibits protein synthesis by ADP-ribosylation of elongation factor 2 (EF-2). This inhibition of protein synthesis leads to cell death and tissue damage, particularly in the respiratory tract and other affected organs (Harapan *et al*., 2019).

Respiratory Symptoms

Respiratory diphtheria typically manifests with symptoms such as sore throat, fever, and the formation of a characteristic thick, grayish membrane in the throat and tonsils. The pseudomembrane consists of necrotic tissue, fibrin and inflammatory cells and adheres tightly to the underlying mucosa.

As the membrane enlarges, it can obstruct the airway, leading to respiratory distress and difficulty in breathing. Other respiratory symptoms may include hoarseness, cough and stridor. In severe cases, respiratory diphtheria can progress rapidly to life-threatening airway obstruction and respiratory failure (WHO, 2017; Harapan *et al*., 2019).

Systemic Complications

In addition to respiratory symptoms, diphtheria toxin can cause systemic effects by disseminating through the bloodstream and targeting various organs and tissues. Systemic complications of diphtheria may include:

1. Myocarditis: Diphtheria toxin can cause myocardial damage, leading to myocarditis and cardiac dysfunction. Manifestations of myocarditis may include chest pain, palpitations, and signs of congestive heart failure such as dyspnea and edema.
2. Neurological Complications: Diphtheria toxin can affect the nervous system, leading to neurotoxicity and neurological complications. Neurological manifestations may include cranial nerve palsies, paralysis and altered mental status.
3. Renal Complications: In rare cases, diphtheria toxin can cause renal dysfunction and acute kidney injury, leading to oliguria, hematuria and electrolyte imbalances.
4. Other Organ Involvement: Diphtheria toxin can also target other organs and tissues, leading to multi-organ dysfunction and systemic illness (Harapan *et al*., 2019; Ibrahim *et al*., 2022).

Figure 2: Illustration depicting several clinical features of Diphtheria. Pseudo-membrane was observed in images A and B, whilst skin lesions were observed in images C and D (Sadoh and Sadoh, 2011).

DIPHTHERIA RISK FACTORS

The disease is influenced by a variety of risk factors that contribute to its transmission and severity. Understanding these risk factors is crucial for implementing effective prevention and control strategies (Sadoh and Sadoh, 2011; Abdulrasheed *et al*., 2023).

Low Vaccination Coverage

Low vaccination coverage is one of the primary risk factors for diphtheria transmission and outbreaks. Vaccination with diphtheria toxoid-containing vaccines, such as the diphtheria-tetanus-pertussis (DTP) vaccine, is highly effective for prevention of diphtheria. However, inadequate vaccination coverage, whether due to vaccine hesitancy, limited access to healthcare services or other factors, can leave populations susceptible to diphtheria infection (Sadoh and Sadoh, 2011; Galadima *et al*., 2021).

Incomplete Immunization

Incomplete immunization, characterized by failure to complete the recommended vaccine series or delayed vaccination, increases the risk of diphtheria among individuals who are not fully protected. Delayed or missed doses of the DTP vaccine can leave individuals vulnerable to diphtheria infection, particularly in areas where the disease is endemic or outbreaks occur sporadically (Galadima *et al*., 2021; Acosta *et al*., 2021)

Travel to Endemic Areas

Travel to regions where diphtheria is endemic or outbreaks are occurring poses a risk of exposure to the bacterium *C. diphtheria.* Individual traveling to countries with low vaccination coverage and inadequate healthcare infrastructure may be at increased risk of diphtheria infection, especially if they have not been adequately vaccinated or received booster doses of the vaccine (NCDC, 2023).

Overcrowding and Poor Hygiene

Overcrowded living conditions and poor hygienic practices facilitate the transmission of diphtheria by providing opportunities for close contact and the spread of respiratory droplets containing *C. diphtheria*. Settings such as schools, daycare centers, and refugee camps are particularly susceptible to diphtheria outbreaks due to crowded living conditions and limited access to healthcare services (NCDC, 2023).

Poor Sanitation

Poor sanitation, including inadequate access to clean water, sanitation facilities and waste management systems, creates environments conducive for the transmission of diphtheria. Contaminated water sources and improper waste disposal can contribute to the spread of *C. diphtheriae,* increasing the risk of infection among susceptible individual (NCDC, 2023).

Age and Immune Status

Young children and older adults, as well as individual with compromised immune systems, are at increased risk of diphtheria infection and severe disease. Children who have not completed the recommended vaccine series are particularly vulnerable to diphtheria, while older adults may experience waning immunity over time. Individual with underlying health conditions or immunodeficiency are also at higher risk of severe diphtheria and complications (WHO, 2017).

RISK ASSESSMENT PROCESS FOR DIPHTHERIA

Risk assessment is a critical component of diphtheria prevention and control efforts, allowing public health authorities to identify populations and settings at increased risk of disease transmission and prioritize interventions accordingly. The risk assessment process involves evaluation of various factors that contribute to the likelihood and severity of diphtheria outbreaks (CDCP, 2016; NCDC, 2023).

Identifying High-Risk Populations and Settings

The first step in the risk assessment process is to identify populations and settings at increased risk of diphtheria transmission. This may include communities with low vaccination coverage, overcrowded living conditions, poor sanitation and limited access to healthcare services. High-risk populations such as young children, older adults and immunocompromised individuals may also be targeted for intervention (CDCP, 2016).

Evaluating Environmental and Socioeconomic Factors

Environmental and socioeconomic factors play a significant role in diphtheria transmission and outbreak risk. Risk assessment involves evaluating factors such as population density, housing conditions, access to clean water and sanitation facilities and socioeconomic status. Communities with poor infrastructure, inadequate healthcare access and socioeconomic disparities are often at higher risk of diphtheria outbreaks (Agrawal *et al*., 2023; NCDC, 2023)

Monitoring Disease Trends and Surveillance Data

Surveillance data are essential for monitoring disease trends and assessing the epidemiological situation of diphtheria in a given area. Public health authorities collect and analyze data on diphtheria cases, vaccination coverage and other relevant indicators to identify trends and patterns of disease transmission. Timely and accurate surveillance data are critical for informing risk assessment and guiding intervention strategies (NCDC, 2023).

Assessing Healthcare Capacity and Resources

The capacity of healthcare systems to detect, diagnose and respond to diphtheria outbreaks is a key consideration in risk assessment. Assessing healthcare capacity involves evaluating factors such as laboratory infrastructure, healthcare workforce availability, access to diagnostic testing, and availability of medical supplies and treatments (NCDC, 2023). Communities with limited healthcare capacity may be at higher risk of diphtheria outbreaks due to challenges in case detection and management (Rintani *et al*., 2018)

Incorporating Risk Communication and Community Engagement

Risk assessment should also consider factors related to risk communication and community engagement. Effective risk communication strategies are essential for informing the public about diphtheria risks, promoting preventive measures such as vaccination, and mobilizing community support for outbreak response efforts. Engaging with communities and stakeholders helps build trust, facilitate collaboration, and enhance the effectiveness of risk assessment and intervention efforts (Besa et al., 2014; CDCP, 2016).

RISK MANAGEMENT STRATEGIES FOR DIPHTHERIA PREVENTION AND CONTROL

Effective risk management is crucial for mitigating the impact of diphtheria outbreaks and preventing the spread of the disease within communities. Risk management strategies encompass a range of interventions aimed at reducing the likelihood of diphtheria transmission, identifying and responding to outbreaks promptly, and minimizing the impact of the disease on affected populations (CDCP, 2016; Clarke, 2017; NCDC, 2023).

Vaccination Programs

Vaccination with diphtheria toxoid-containing vaccines, such as the diphtheria-tetanus-pertussis (DTP) vaccine, is the cornerstone of diphtheria prevention efforts. Risk management strategies include:

i. Ensuring high vaccination coverage rates among target populations, including infants, children, and adults.
ii. Implementing catch-up vaccination campaigns to reach underserved communities and individuals who may have missed routine vaccinations.
iii. Providing booster doses of the vaccine to maintain immunity over time, particularly in populations at higher risk of diphtheria infection.
iv. Addressing vaccine hesitancy and improving vaccine acceptance through targeted communication campaigns and community engagement efforts (CDCP, 2016; UNICEF 2021).

Isolation and Quarantine

Isolation and quarantine are critical measures for preventing the spread of diphtheria during outbreaks. Risk management strategies include:

i. Isolating individuals with suspected or confirmed diphtheria cases to prevent further transmission of the disease.
ii. Implementing quarantine measures for individuals who have been exposed to diphtheria cases to prevent secondary transmission.
iii. Enforcing strict infection control measures in healthcare settings, including use of personal protective equipment and adherence to hand hygiene protocols (NCDC, 2023).

Treatment and Medical Interventions

Early detection and prompt treatment of diphtheria cases are essential for reducing morbidity and mortality associated with the disease. Risk management strategies include:

i. Providing timely access to medical care for individuals with suspected or confirmed diphtheria cases.
ii. Administering antibiotics, such as erythromycin or penicillin, to treat diphtheria infections and prevent complications.
iii. Administering diphtheria antitoxin, when available, to neutralize circulating diphtheria toxin and reduce disease severity.
iv. Monitoring patients closely for signs of respiratory compromise, myocarditis, and other complications, and providing supportive care as needed (NCDC, 2023; Olulaja *et al*., 2023).

Surveillance and Early Detection

Robust surveillance systems are essential for early detection of diphtheria cases and outbreaks. Risk management strategies include:

i. Monitoring disease trends and collecting epidemiological data to identify clusters of diphtheria cases and assess outbreak risks.
ii. Conducting laboratory testing to confirm diphtheria diagnoses and characterize circulating strains of *C. diphtheriae*.
iii. Implementing active surveillance measures, such as case reporting and contact tracing, to identify and isolate individuals with suspected or confirmed diphtheria cases promptly (NCDCP, 2023).

Enhancing Hygiene Practices

Promoting good hygiene practices is essential for preventing diphtheria transmission and reducing the risk of infection. Risk management strategies include:

i. Educating the public about the importance of hand hygiene, respiratory etiquette, and environmental sanitation in preventing diphtheria.
ii. Promoting regular handwashing with soap and water, especially after coughing, sneezing, or using the restroom.
iii. Encouraging individuals to cover their mouth and nose with a tissue or elbow when coughing or sneezing to prevent the spread of respiratory droplets.
iv. Implementing environmental cleaning and disinfection measures in high-risk settings, such as schools, healthcare facilities, and communal living spaces (CDCP, 2016; NCDC, 2023).

CHALLENGES IN DIPHTHERIA SURVEILLANCE AND REPORTING

Effective surveillance and reporting systems are critical for monitoring disease trends, detecting outbreaks, and implementing timely interventions to control diphtheria. However, several challenges hinder the ability of public health authorities to conduct comprehensive surveillance and reporting of diphtheria cases. This section explores the challenges associated with incomplete data collection, lack of centralized reporting, and diagnostic challenges in diphtheria surveillance and reporting (Truelove *et al*., 2020; NCDC, 2023).

Incomplete Data Collection

One of the primary challenges in diphtheria surveillance is incomplete data collection, which can result from various factors:

i. Underreporting of Cases: Diphtheria cases may go unreported due to limited access to healthcare services, lack of awareness among healthcare providers, or failure to recognize and diagnose the disease.
ii. Inaccurate Case Documentation: Incomplete or inaccurate documentation of diphtheria cases in medical records and surveillance databases can lead to discrepancies in reported case numbers and hinder accurate assessment of disease burden.
iii. Fragmented Reporting Systems: Fragmentation of reporting systems at the local, regional, and national levels can result in inconsistencies in data collection and reporting practices, making it challenging to compile comprehensive surveillance data (Truelove *et al*., 2020).

Lack of Centralized Reporting

The lack of centralized reporting mechanisms poses a significant challenge to diphtheria surveillance and reporting:

i. Fragmented Reporting Channels: Diphtheria cases may be reported through multiple channels, including healthcare facilities, laboratories, and public health agencies, leading to fragmentation and duplication of reporting efforts.
ii. Communication Gaps: Inadequate communication and coordination among reporting entities can result in delays in data sharing and response coordination, hindering timely detection and control of diphtheria outbreaks.
iii. Data Silos: Information may be siloed within different reporting systems and agencies, making it difficult to aggregate and analyze data comprehensively for surveillance purposes (NCDC, 2023).

Diagnostic Challenges

Diagnostic challenges present additional obstacles to effective diphtheria surveillance and reporting:

i. Laboratory Capacity: Limited laboratory capacity for diphtheria diagnosis, particularly in resource-limited settings, can result in delays in case confirmation and reporting.
ii. Availability of Diagnostic Tests: Access to diagnostic tests for diphtheria, such as culture and polymerase chain reaction (PCR) assays, may be limited in some regions, further complicating case detection and confirmation.
iii. Differential Diagnosis: Diphtheria can mimic other respiratory infections, leading to challenges in clinical diagnosis and accurate case identification (Truelove *et al*., 2020; NCDC, 2023).

CLINICAL DIAGNOSIS AND LABORATORY CONFIRMATION OF DIPHTHERIA

Early detection and accurate diagnosis of diphtheria are essential for initiating timely treatment and implementing control measures to prevent further transmission of the disease. Clinical diagnosis relies on the recognition of characteristic signs and symptoms, while laboratory confirmation through bacterial culture or polymerase chain reaction (PCR) testing is essential for confirming diphtheria cases. This section provides a comprehensive overview of clinical diagnosis and laboratory confirmation methods for diphtheria (Harapan *et al*., 2019; CDCP, 2024).

Clinical Diagnosis

Clinical diagnosis of diphtheria is based on the recognition of characteristic signs and symptoms, which may include:

i. Sore Throat: Diphtheria often presents with a sore throat, which may be mild initially but can progress rapidly.

ii. Difficulty Swallowing: Dysphagia or difficulty swallowing may occur due to the presence of a thick grayish membrane in the throat.
iii. Characteristic Membrane: The hallmark of respiratory diphtheria is the formation of a thick grayish membrane composed of necrotic tissue, fibrin, and inflammatory cells in the throat and tonsils. This membrane adheres tightly to the underlying mucosa and may extend into the airway, leading to respiratory compromise.
iv. Systemic Symptoms: Patients with severe diphtheria may also experience systemic symptoms such as fever, malaise, and lymphadenopathy.

Clinical suspicion of diphtheria should prompt healthcare providers to initiate appropriate diagnostic testing and implement infection control measures to prevent further transmission of the disease (Harapan *et al*., 2019; CDCP, 2024).

Laboratory Confirmation

Laboratory confirmation of diphtheria is essential for confirming the diagnosis and guiding treatment decisions. The following laboratory tests are commonly used for diphtheria confirmation:

i. Bacterial Culture: The gold standard for diphtheria diagnosis is isolation of *C. diphtheriae* from clinical specimens, such as throat swabs or membrane samples. Specimens are plated on selective media, and colonies characteristic of *C. diphtheriae* are identified based on morphology and biochemical tests.
ii. Polymerase Chain Reaction (PCR) Testing: PCR assays can detect the presence of *C. diphtheriae* DNA in clinical specimens with high sensitivity and specificity. PCR testing is particularly useful for rapid diagnosis of diphtheria and may be employed in settings where bacterial culture is not readily available or for confirmation of equivocal culture results.
iii. Testing for Toxigenicity: In addition to identifying the presence of *C. diphtheriae* in clinical specimens, it is essential to determine toxigenicity, as not all strains of *C. diphtheriae* produce the diphtheria toxin. Toxigenicity testing involves:

a) Elek Test: The Elek test is a classic method for detecting diphtheria toxin production. It involves inoculating a filter paper strip impregnated with specific antitoxin against diphtheria toxin with a culture of *C. diphtheriae*. If the bacterium produces toxin, a precipitin line forms where the toxin and antitoxin interact.
b) PCR for Tox Gene: Polymerase chain reaction (PCR) assays targeting the tox gene, which encodes the diphtheria toxin, can detect toxigenic strains of *C. diphtheriae*. PCR testing provides rapid and sensitive detection of toxigenicity and is increasingly used in diagnostic laboratories for diphtheria confirmation (Harapan *et al*., 2019; Agrawal *et al*., 2023)

DIPHTHERIA PREVENTIVE MEASURES

Preventing diphtheria relies on a multifaceted approach that includes vaccination, early detection of cases, improved sanitation practices, and community engagement. By implementing comprehensive preventive measures, public health authorities can reduce the incidence of diphtheria and mitigate its impact on affected populations (WHO, 2017; Truelove *et al*., 2020).

Vaccination

Vaccination with diphtheria toxoid-containing vaccines, such as the diphtheria-tetanus-pertussis (DTP) vaccine, is the most effective preventive measure against diphtheria. Key aspects of vaccination for diphtheria prevention include:

i. Routine Vaccination: Ensuring that infants and children receive the recommended doses of the DTP vaccine according to national immunization schedules.
ii. Booster Doses: Administering booster doses of the vaccine to maintain immunity over time, particularly in adolescents and adults who may be at risk of waning immunity.

iii. Catch-up Vaccination: Implementing catch-up vaccination campaigns to reach underserved populations and individuals who may have missed routine vaccinations.

iv. Vaccine Coverage: Achieving and maintaining high vaccination coverage rates among target populations to establish herd immunity and prevent diphtheria outbreaks (WHO, 2017; Acosta *et al*., 2021).

Early Detection

Early detection of diphtheria cases is essential for implementing timely interventions to prevent further transmission of the disease. Key components of early detection include:

i. Clinical Surveillance: Training healthcare providers to recognize the signs and symptoms of diphtheria, including sore throat, difficulty swallowing, and the presence of a characteristic thick gray membrane in the throat.

ii. Laboratory Confirmation: Conducting prompt laboratory testing, including bacterial culture and polymerase chain reaction (PCR) assays, to confirm diphtheria diagnoses and guide treatment decisions.

iii. Active Surveillance: Implementing active surveillance measures, such as case reporting and contact tracing, to identify and isolate individuals with suspected or confirmed diphtheria cases and prevent secondary transmission (Truelove *et al*., 2020).

Improved Sanitation Practices

Improving sanitation practices can help reduce the transmission of diphtheria and other infectious diseases. Key aspects of sanitation for diphtheria prevention include:

i. Access to Clean Water: Ensuring access to safe and clean drinking water to prevent contamination and transmission of *C. diphtheriae*.

ii. Sanitation Facilities: Promoting the use of proper sanitation facilities, including toilets and handwashing stations, to minimize the spread of infectious agents.

iii. Waste Management: Implementing effective waste management systems to reduce environmental contamination and prevent the proliferation of disease vectors (WHO, 2017; Truelove *et al*., 2020).

Community Engagement

Community engagement plays a crucial role in diphtheria prevention efforts by fostering awareness, promoting vaccination uptake, and encouraging adherence to preventive measures. Key strategies for community engagement include:

i. Health Education: Conducting health education campaigns to raise awareness about diphtheria risks, symptoms, and preventive measures, including vaccination and good hygiene practices.

ii. Community Outreach: Engaging with community leaders, stakeholders, and influencers to mobilize community support for diphtheria prevention initiatives and address barriers to vaccination and healthcare access.

iii. Partnerships: Collaborating with local organizations, schools, religious institutions, and other community-based entities to promote diphtheria prevention and control activities and reach underserved populations (WHO, 2017; Joel, 2023).

EFFECTIVE DIPHTHERIA CASE MANAGEMENT AND TREATMENT

Diphtheria is a serious bacterial infection, characterized by the formation of a thick grayish membrane in the throat and respiratory tract. Prompt and appropriate case management is essential for reducing morbidity and mortality associated with diphtheria and preventing further transmission of the disease (Obanewa and Newell, 2020, NCDC, 2023).

Isolation and Infection Control

Upon suspicion or confirmation of diphtheria, patients should be promptly isolated to prevent further transmission of the disease. Key components of isolation and infection control include:

i. Respiratory Precautions: Implementing respiratory precautions, such as placing patients in airborne infection isolation rooms or using surgical masks, to minimize the spread of respiratory droplets containing *C. diphtheriae*.
ii. Contact Precautions: Enforcing contact precautions, including hand hygiene and use of personal protective equipment, for healthcare providers and caregivers who come into contact with diphtheria patients or potentially contaminated materials.
iii. Environmental Cleaning: Thoroughly cleaning and disinfecting patient care areas and equipment to reduce environmental contamination and prevent transmission of *C. diphtheriae* to other individuals (Obanewa and Newell, 2020)

Antimicrobial Therapy

Antimicrobial therapy is a cornerstone of diphtheria treatment and aims to eradicate the causative bacteria and prevent complications. Key aspects of antimicrobial therapy for diphtheria include:

i. Antibiotics: Administering antibiotics, such as erythromycin or penicillin, to eradicate *C. diphtheriae* and prevent the production of diphtheria toxin. Antibiotic therapy should be initiated promptly upon suspicion or confirmation of diphtheria and continued for a minimum of 14 days to ensure complete eradication of the bacteria.
ii. Diphtheria Antitoxin: Administering diphtheria antitoxin to neutralize circulating diphtheria toxin and mitigate its effects on affected tissues and organs. Diphtheria antitoxin should be administered as soon as possible after diagnosis to prevent the progression of disease and reduce morbidity and mortality associated with diphtheria (Ibrahim *et al*., 2022; NCDC, 2023)

Supportive Care

Supportive care plays a crucial role in managing diphtheria cases and alleviating symptoms associated with the disease. Key components of supportive care include:

i. Airway Management: Monitoring patients closely for signs of respiratory compromise, such as stridor or difficulty breathing, and providing appropriate interventions, including supplemental oxygen and mechanical ventilation, as needed.
ii. Fluid and Nutritional Support: Ensuring adequate hydration and nutrition for patients, especially those with severe diphtheria who may experience difficulty swallowing or respiratory distress. Enteral or parenteral nutrition may be necessary for patients unable to tolerate oral intake.
iii. Monitoring for Complications: Monitoring patients for complications of diphtheria, such as myocarditis, neurologic sequelae, and airway obstruction, and providing timely interventions to prevent or manage these complications (Clarke, 2017; Obanewa and Newell, 2020).

Follow-Up and Surveillance

After initial treatment, patients with diphtheria should undergo regular follow-up evaluations to monitor their clinical progress and ensure complete resolution of symptoms. Key components of follow-up and surveillance include:

i. Clinical Monitoring: Monitoring patients for signs of disease recurrence, complications, or treatment-related adverse events during follow-up visits.
ii. Laboratory Testing: Conducting laboratory testing, such as bacterial culture and toxin testing, to confirm eradication of *C. diphtheriae* and assess the effectiveness of antimicrobial therapy.
iii. Public Health Reporting: Reporting confirmed cases of diphtheria to public health authorities for surveillance purposes and implementation of control measures to prevent further transmission of the disease within the community (Truelove *et al*., 2020; NCDC, 2023).

RECOMMENDATIONS FOR DIPHTHERIA CONTROL

Based on the comprehensive overview of diphtheria prevention, diagnosis and management, several recommendations can be made to enhance efforts in controlling the spread of the disease and reducing its impact:

1. Vaccination Programs: Ensure that vaccination programs are accessible, affordable, and widely available to all populations, with a focus on maintaining high vaccination coverage rates among infants, children, adolescents, and adults. Implement catch-up vaccination campaigns to reach underserved communities and individuals who may have missed routine vaccinations.
2. Enhanced Surveillance: Strengthen surveillance systems for early detection of diphtheria cases and outbreaks, including active surveillance measures such as case reporting and contact tracing. Improve laboratory capacity for diphtheria diagnosis, including bacterial culture and PCR testing, to facilitate timely confirmation of cases and guide treatment decisions.
3. Community Engagement: Engage with communities through targeted health education campaigns, community outreach activities, and partnerships with local organizations to raise awareness about diphtheria risks, symptoms, and preventive measures. Foster trust and collaboration to promote vaccination uptake, early detection of cases, and adherence to infection control measures.
4. Healthcare Capacity Building: Enhance healthcare capacity and resources for diphtheria case management and treatment, including training healthcare providers in clinical recognition, diagnosis, and management of diphtheria cases. Ensure availability of essential medical supplies, antibiotics, diphtheria antitoxin, and supportive care interventions to optimize patient outcomes.
5. Improved Sanitation: Invest in improved sanitation infrastructure and practices to minimize environmental contamination and reduce the risk of diphtheria transmission. Ensure access to clean water, proper sanitation facilities, and effective waste management systems to promote public health and prevent the spread of infectious diseases.
6. Research and Development: Support research and development efforts to improve diphtheria diagnostics, therapeutics, and vaccines. Invest in innovative approaches for diphtheria prevention and control, including novel vaccine technologies, antimicrobial agents, and public health interventions to address emerging challenges and evolving epidemiological trends (CDCP, 2016; WHO, 2017; NCDC, 2023).

CONCLUSION

The management and prevention of diphtheria demand a comprehensive and multifaceted approach. Through vaccination programs, early detection, improved sanitation and community engagement, significant strides can be made in reducing the incidence of diphtheria and mitigating its impact on public health. Vaccination remains the cornerstone of prevention efforts, with emphasis on maintaining high coverage rates and implementing catch-up campaigns to reach vulnerable populations. Early detection through robust surveillance systems and prompt laboratory confirmation is crucial for initiating timely interventions and preventing further transmission of the disease. Additionally, investments in sanitation infrastructure and hygiene practices can help minimize environmental contamination and reduce the risk of diphtheria transmission. Community engagement and partnerships play a significant role in raising awareness, promoting vaccination uptake, and fostering collaboration in diphtheria prevention and control efforts.

Furthermore, effective case management and treatment are essential for reducing morbidity and mortality associated with diphtheria. Isolation and infection control measures, antimicrobial therapy, diphtheria antitoxin administration, and supportive care are key components of comprehensive case management procedures. Regular follow-up and surveillance ensure the continued monitoring of patients' clinical progress and the effectiveness of interventions.

Conflict of interest: The authors declare that there are no conflicts of interest

Authors' contributions

ADA designed the study and drafted the first manuscript. OMO, AAF and HM designed and reviewed the final manuscript for intellectual content. All authors contributed to the final version of the manuscript and are responsible for the integrity and accuracy of this review

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