



EPIDEMIOLOGY OF DIPHTHERIA INFECTION AMONG DEMOGRAPHIC CHARACTERISTICS: A SYSTEMATIC REVIEW

¹Adegwu O. Lewis, ²Dr. Akyala A.I ³Dr. Ngwai Y.B ⁴Dr. Salihu Abdullahi, ⁵Dr. Bassey Enya Bassey, ⁶Dr. Eshetu Wassie, ⁷Dr. Mahdi Musa, ⁸Dr. Asma'i Zeenat Kabir, ⁹Dr. Abba Ahmed Danzomo, and ¹⁰ Mr. Abah Micheal Idoko

¹⁻³Department of Public Health, Global Health and Infectious Disease Institute,
University, Keffi, Nasarawa State.,

⁴⁻⁸ World Health Organizationn,

⁹BMGF & GAVI and

¹⁰Nasarawa State University, Keffi

Abstract: Diphtheria, a vaccine-preventable disease, has re-emerged globally, particularly in regions with fragile health systems, low immunisation coverage, and post-pandemic service disruptions. To better understand its burden across demographic groups, a systematic review was conducted to synthesise evidence on the epidemiology, clinical features, and outcomes of diphtheria. Studies published between 2018 and 2025 were reviewed, including peer-reviewed articles, surveillance reports, and outbreak investigations. Seventeen studies from Africa, Asia, Europe, and global datasets were included. In Nigeria, large-scale outbreaks were reported post-COVID-19, with Kano State alone contributing 85% of national cases, and mortality was highest among unvaccinated individuals or those with delayed access to treatment. Across Asia, particularly in India and Indonesia, children aged 6–10 years from low socioeconomic backgrounds were most affected, with case fatality rates ranging between 5.8% and 13%. Risk factors consistently included incomplete vaccination, delayed access to diphtheria antitoxin, and weak surveillance systems. Studies from Europe highlighted re-emergence among migrants and refugees, while genomic epidemiology demonstrated multiple *Corynebacterium diphtheriae* lineages linked to low coverage. Overall, the evidence underscores diphtheria's persistence as a public health challenge in resource-limited settings and among vulnerable populations, highlighting the urgent need for strengthened routine immunisation, timely availability of antitoxin, and improved genomic and epidemiological surveillance to mitigate future outbreaks.

Keywords: Age-specific, diphtheria, demographic, distribution, epidemiology, gender, infection,

INTRODUCTION

Diphtheria is a life-threatening bacterial infection caused primarily by *Corynebacterium diphtheriae*, a Gram-positive, non-motile bacterium that produces a lethal exotoxin under the influence of temperate bacteriophages (Adegboro, 2021; Prygiel et al., 2022). Diphtheria remains one of the causes of infant and toddler mortality due to low immunity, although it is a vaccine-preventable disease (PD3I) (Ministry of Health RI, 2018). Between 2000 and 2016, Indonesia ranked among the top ten countries

worldwide with the highest number of diphtheria cases and occupied the second-highest position among SEARO (South-East Asia Region) member countries (Arifin & Prasasti, 2017).

The classical and most severe clinical presentation of diphtheria involves the respiratory tract and ENT region, manifesting as pseudomembranous pharyngitis and laryngeal obstruction ("croup"), which accounts for 10–30% of reported cases. However, cutaneous infections are more common, representing 57–86% of cases in the

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literature, and play an important role in the epidemiology of the disease (Bernard et al., 2019). These two presentations are not mutually exclusive (Albato *et al.*, 2021) and may be associated with pharyngeal or cutaneous colonization. Disease severity is linked to diphtheria toxin, which can disseminate beyond the primary infection site, leading to cardiac and neurological complications. This toxin syndrome is particularly frequent in ENT infections but can also occur in cutaneous forms (Martini et al., 2019). Fortunately, tox strains predominate in France, accounting for approximately 90% of isolates (Alberto et al., 2021)

This highly contagious disease primarily affects the respiratory tract and has historically been a major cause of childhood mortality worldwide (Zakikhany & Efstratiou, 2012). The pathogen exists in three distinct strains identifiable on tellurite agar: *gravis* (3-5mm), *mitis* (2-4mm), and *intermedius* (1-2mm), with only toxigenic strains capable of producing the characteristic diphtheria toxin that blocks cellular protein synthesis and creates the distinctive pseudo-membrane at infection sites (Adegboro, 2021; Prygiel et al., 2022). Respiratory diphtheria is primarily transmitted via respiratory droplets, with the risk of contamination depending on clinical presentation and carriage status. Nevertheless, direct contact through skin lesions is considered the most frequent route of transmission (Chandhary and Pandey, 2022), while indirect transmission through contaminated objects is also possible (Truelove et al., 2020). In contrast, *C. ulcerans* is a zoonotic pathogen, transmitted mainly by domestic animals (cats and dogs) and, less commonly, through consumption of unpasteurized milk (Martini et al., 2019). However, concerning resurgences that have emerged globally, the incidence of diphtheria in Indonesia has shown an increasing trend each year. In 2015, 415 cases and 24 deaths were reported, while in 2016, the case fatality rate (CFR) reached 5.8%. East Java province has recorded the highest incidence of diphtheria over the years. In 2011 and 2012, all districts and cities in East Java experienced outbreaks (Izza & Soenarnatalina, 2015). Another outbreak occurred in 2016, with six deaths reported (Ministry of Health RI, 2018). In 2017, diphtheria cases in East Java rose to 460, with 16 deaths, and further

increased to 758 cases with three deaths in 2018 (East Java Provincial Health Office, 2018). Over the past two decades, diphtheria has re-emerged in several developed countries, including France (Burkovski, 2013; Martini *et al.*, 2019). Recent cases have mainly involved vulnerable populations with comorbidities, as well as travelers from endemic regions such as India, Madagascar, Indonesia, Africa, and the former USSR (Alberto *et al.*, 2021; Chaudhary and Pandey, 2022).

Nigeria recorded 1,870 diphtheria cases in 2018; however, there were over 20,000 cases reported in 2019. This occurred despite the World Health Organisation's report of a decline in infections from 100,000 in 1980 to fewer than 10,000 in 2021. On January 23, 2023, the Nigerian Centre for Disease Control (NCDC, 2023) announced a diphtheria epidemic affecting four of Nigeria's 36 states, reporting 128 confirmed cases and 38 fatalities. This information was revealed 18 days following the NCDC's report of 189 fatalities linked to Lassa fever and 63 cases of Lassa fever among healthcare professionals in 2022 (NCDC, 2023). In February 2023, there were 216 reported cases of diphtheria, leading to 40 fatalities within a span of less than one month. The NCDC (2023) has reported 523 suspected cases across Kano, Yobe, Katsina, Lagos, and Osun states. Kano reported the highest number of suspected cases at 396, with 211 confirmed cases and 38 fatalities. Yobe had 78 suspected cases and two confirmed cases. Katsina recorded 34 suspected cases. Lagos reported 14 suspected cases, two confirmed cases, and two fatalities. Osun state reported one case with no fatalities. The mortality rate stood at 18.5%, affecting both genders, with the majority of confirmed cases (85.2%) occurring in children aged 2 to 14. The northern region of the country seems to exhibit a higher prevalence of the epidemic.

Diphtheria manifests in respiratory and non-respiratory forms, with respiratory variants carrying higher mortality risks (Acosta et al., 2021). The disease typically presents with an incubation period of 2-10 days, followed by symptoms including mild fever, pharyngitis, and the formation of characteristic pseudomembranes (Acosta et al., 2021). Severe cases can progress to "bull-neck" diphtheria with significant cervical lymphadenopathy and potential airway obstruction. Systemic complications



include myocarditis, polyneuropathies, and respiratory failure due to toxin-mediated damage to cardiac conduction systems and respiratory muscles (Adegboro, 2021; Besa *et al.*, 2014). The recent outbreaks coincide with the identification of non-toxigenic tox gene-bearing (NTTB) strains of *C. diphtheriae*, which carry the toxin gene but do not express it, raising concerns about their potential for toxigenic conversion (Prygiel *et al.*, 2022). Additionally, other *Corynebacterium* species, including *C. ulcerans* and *C. pseudotuberculosis*, have demonstrated the capability to produce exotoxins, complicating the epidemiological landscape (Adegboro, 2021).

According to Ibrahim *et al.* (2024) that a higher incidence of diphtheria-related fatalities was observed in individuals under 5 years of age (7.7%) and in female cases (5.9%). Rural habitation (7.7%) and the North-eastern senatorial district (8.2%) documented a higher number of fatalities than cases from the urban regions and other senatorial districts of the state. Substantially elevated mortality rates were seen in cases (presumptive/clinically diagnosed) for which samples were not collected for laboratory analysis (10.0%, $P = 0.002$). The likelihood of fatality associated with diphtheria was elevated among presumptive or clinically identified cases. Individuals with diphtheria from whom samples were collected had a 10% reduced likelihood of mortality from the disease (adjusted odds ratio = 0.1; 95% confidence interval = 0.01–0.6) compared to those without sample collection, which were considered demographic factors associated with diphtheria infection in the region.

Prevention efforts through immunisation have been insufficient to fully control diphtheria cases (Clarke, 2017). Programs such as Outbreak Response Immunisation (ORI), Backlog Fighting (BLF), and National Immunisation Week (PIN) were implemented to anticipate outbreaks; however, diphtheria cases continued to rise. This persistent increase has been linked to inadequate immunisation coverage, particularly the failure to achieve full coverage of the seven recommended diphtheria doses (East Java Provincial Health Office, 2018). The need to review previous studies systematically is because there are tendencies of epidemiological deficiencies in comprehending demographic factors of diphtheria

infection dynamics. Therefore, this study employed a systematic review methodology to investigate the epidemiology of diphtheria in relation to demographic characteristics and the trend of infection with below questions and objectives:

Research Questions

1. What is the distribution of diphtheria cases across different geographical regions and countries?
2. What are the age-specific incidence rates and case fatality rates of diphtheria infection?
3. What are the gender-specific differences in diphtheria incidence, severity, and mortality rate?

Objectives:

1. To determine the global distribution of diphtheria cases across different geographical regions.
2. To determine the age-specific incidence rate and case fatality rate of diphtheria infection.
3. To determine the gender-specific differences in diphtheria incidences, severity and mortality.

MATERIALS AND METHODS

This study employed a systematic review approach, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Relevant literature was searched, identified, screened, and selected through the PRISMA flow process (identification, screening, eligibility, exclusion, and inclusion), as illustrated in Figure 1.

The primary databases searched included Google Scholar, PubMed, and Scopus, as they provide broad access to peer-reviewed articles and epidemiological studies. Search strings combined Medical Subject Headings (MeSH) and free-text terms related to diphtheria and demographics. The following key terms and Boolean operators were applied: (“diphtheria” OR “*Corynebacterium diphtheriae*” OR “diphtheria infection”) AND (“epidemiology” OR “incidence” OR “prevalence”) AND (“age” OR “sex” OR “gender” OR “education” OR “socioeconomic status” OR “demographic characteristics”). Synonyms were included using a thesaurus and references from previous systematic reviews to ensure comprehensive coverage. The literature search identified 36 records from database searching and



manual screening (Google Scholar, PubMed, Scopus). After removing 5 duplicates, 31 unique records underwent title and abstract screening. Following screening, 14 records were excluded for not meeting the study scope or eligibility criteria. Seventeen full-text articles were assessed and met the inclusion criteria for qualitative synthesis. The study selection process is summarized in the PRISMA flow diagram (Figure 1). Data abstraction involved extracting information on study setting,

population, demographic variables, diphtheria incidence, mortality, case fatality rate, and immunization status. Each included study was read in detail, and findings were synthesized thematically to address the research objectives. The themes and sub-themes were systematically organized and presented in relation to the epidemiological characteristics of diphtheria infection across different demographic groups (Table 2).

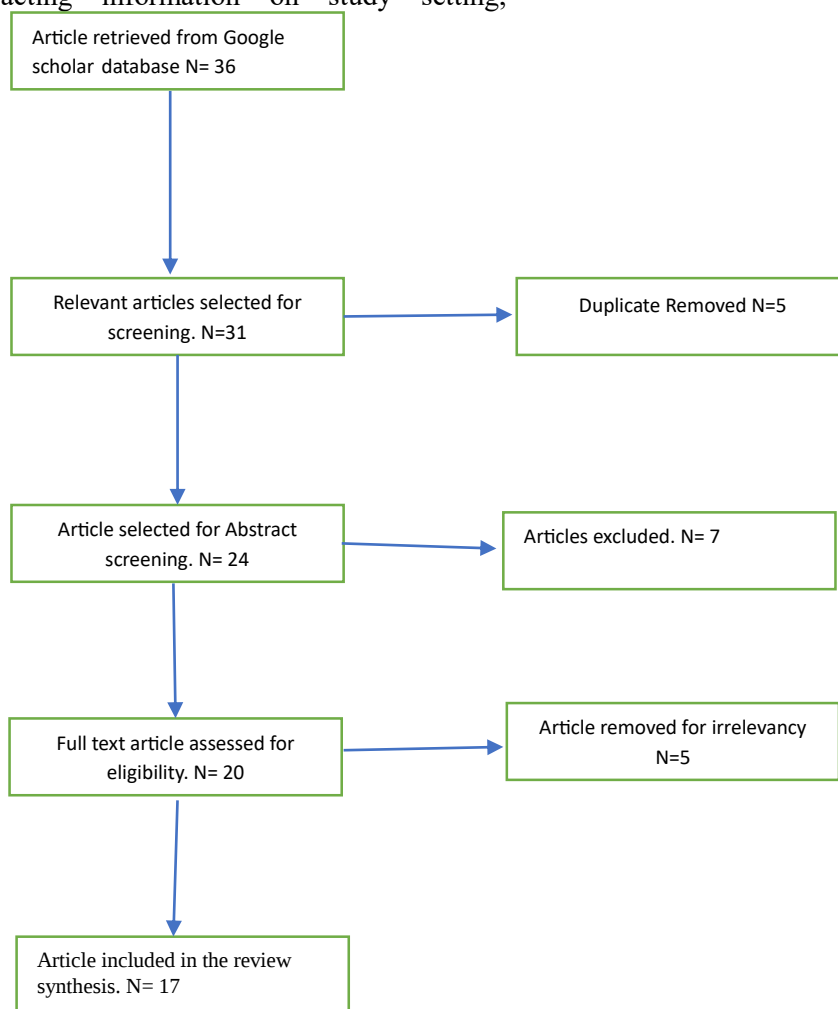




Figure 1: PRISMA flow diagram of Systematic Review

Table 1. Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Studies published between 2018–2025	Publications before the chosen start year
English language articles	Non-English articles (unless translated)
Human studies reporting epidemiologic data on diphtheria	Animal studies, in vitro studies, or basic microbiology without epidemiologic data
Peer-reviewed articles, official surveillance reports, outbreak investigations	Commentaries, editorials, narrative reviews without primary data
Empirical designs (surveillance, cross-sectional, cohort, outbreak investigations, case series with population denominators)	Single case reports without denominators or insufficient demographic data



Table 2. SUMMARY OF STUDIES INCLUDED IN THIS REVIEW

Author(s) & Year	Country/Region	Study Objectives	Participants/Sample Size	Data Source	Study Design/Methods	Key Findings
Abbas et al., 2025	Nigeria (Kano State)	To analyze post-COVID-19 diphtheria resurgence and identify mortality-related risk factors	18,320 confirmed cases (February 2022–April 2024)	SORMAS surveillance database	Descriptive epidemiology with logistic regression analysis	The findings revealed that the outbreak represented 85% of Nigeria's total diphtheria burden with a CFR of 4.5%. Unvaccinated patients demonstrated 2.45× higher odds of mortality compared to fully vaccinated individuals
Ogunleye et al., 2023	Nigeria (27 states)	To advocate for participatory epidemiology in diphtheria outbreak response and highlight surveillance system gaps	~4,160 suspected cases; 1,532 laboratory-confirmed cases	NCDC surveillance reports and editorial synthesis	Narrative review and participatory epidemiology editorial	The findings showed a national CFR of 8.9%, with 81.9% of confirmed cases occurring among unvaccinated children aged 2–14 years. The study emphasized inadequate surveillance infrastructure and vaccine hesitancy as critical challenges



Usamatu et al., 2025	Nigeria (Sokoto, North-West region)	To assess diphtheria mortality patterns and clinical management outcomes in hospitalized patients	98 consecutive hospitalized cases	Hospital case records from Usmanu Danfodiyo University Teaching Hospital (UDUTH)	Retrospective clinical review	The findings indicated elevated mortality rates with primary contributing factors including delayed clinical presentation, limited access to diphtheria antitoxin (DAT), and incomplete immunization status. The study reinforced the critical need for timely antitoxin administration and comprehensive vaccination coverage
Ministry of Health RI, 2018	Indonesia (nationwide)	To document national diphtheria disease burden and characterize outbreak patterns	National population-level data	National disease surveillance reports	Descriptive epidemiological analysis	The findings documented that Indonesia ranked second highest in diphtheria incidence within the SEARO region, with a national CFR of 5.8% in 2016
Clarke, 2017	Multiple countries (global analysis)	To evaluate effectiveness of Outbreak Response Immunization (ORI) strategies	Outbreak-affected populations across multiple settings	WHO and Ministry of Health outbreak reports	Systematic review and programmatic evaluation	The findings demonstrated that ORI interventions showed insufficient effectiveness in



							settings with low baseline immunization coverage
Wagner et al., 2018	Yemen (conflict-affected regions)	To characterize diphtheria outbreak epidemiology during humanitarian crisis	1,516 cases	confirmed	WHO outbreak investigation reports	Descriptive epidemiological analysis	The findings revealed that the outbreak disproportionately affected children under 15 years due to severely disrupted routine immunization services during conflict
Edmunds et al., 2019	India (multiple states)	To examine demographic and immunological factors contributing to diphtheria resurgence	>2,000 cases	confirmed	National disease surveillance system	Epidemiological analysis with demographic stratification	The findings identified that adolescents and young adults were most severely affected due to waning vaccine-induced immunity over time
Kamble et al., 2024	India (Delhi)	To analyze clinical-epidemiological profile and outcomes of diphtheria patients	94 patients	hospitalized	Hospital case records and structured questionnaires	Cross-sectional observational study	The findings showed a mean patient age of 9 years, with only 6.4% having complete vaccination history and a CFR of 13%. Major complications included neuropathy



						(22%), cardiac involvement (13%), and respiratory complications (14%). Delayed clinical presentation was strongly associated with adverse outcomes
Dureab et al., 2020	Bangladesh (Rohingya refugee camps)	To describe diphtheria epidemiological patterns in displaced populations	>7,000 confirmed cases	WHO and camp health facility surveillance data	Outbreak investigation and descriptive analysis	The findings documented exceptionally high incidence rates among refugee children with critically low vaccination coverage and overcrowded living conditions
Berger et al., 2021	Europe (multiple countries)	To assess diphtheria re-emergence patterns in migrant and traveler populations	Multiple imported cases across European countries	European Centre for Disease Prevention and Control (ECDC) surveillance networks	Retrospective surveillance review	The findings identified cases predominantly among migrants and refugees originating from diphtheria-endemic countries, highlighting importation risks
Hadfield et al., 2022	Global (multi-continental)	To analyze genomic epidemiology and transmission patterns of	Global collection of bacterial isolates	Whole genome sequencing databases	Phylogenomic and molecular epidemiological analysis	The findings revealed multiple distinct <i>C. diphtheriae</i> lineages circulating globally, with



*Corynebacteriu
m diphtheriae*

outbreak
clusters strongly
correlated with
regions of
suboptimal
vaccination
coverage

Abbreviations: CFR = Case Fatality Rate; DAT = Diphtheria Antitoxin; ECDC = European Centre for Disease Prevention and Control; NCDC = Nigeria Centre for Disease Control; ORI = Outbreak Response Immunisation; SEARO = South-East Asia Regional Office; SORMAS = Surveillance Outbreak Response Management and Analysis System; UDUTH = Usmanu Danfodiyo University Teaching Hospital; WHO = World Health Organisation

RESULTS AND DISCUSSION

Distribution of Diphtheria Cases

Table 3. Distribution of Diphtheria Cases

Region/Country	Reference(s)	Key Observations
Nigeria (Kano, Sokoto, 27 states)	Abbas et al. 2025; Ogunleye et al. 2023; Usamatu et al. 2025	Kano State accounted for 85% of national cases in the post-COVID-19 period; CFR ranged from 4.5%–9%. Mortality was highest among unvaccinated children.
India (Delhi, National)	Kamble et al. 2024; Edmunds et al. 2019	The majority of cases occurred among children aged 6–10 years; CFR = 13%. Evidence of waning immunity among adolescents and adults was documented.
Indonesia (East Java, National)	Rahmawati & Wahyuni 2014; Izza & Soenarnatalina 2015; Triana 2016	Repeated outbreaks were linked to incomplete DPT3 vaccination coverage. Unvaccinated children were 5× more likely to contract diphtheria compared to vaccinated peers.
Bangladesh (Rohingya camps)	Dureab et al. 2020	Over 7,000 cases were documented among displaced populations, with exceptionally high incidence rates among poorly immunized children in overcrowded conditions.
Yemen	Wagner et al. 2018	Outbreaks primarily affected children under 15 years in conflict-affected regions where routine vaccination services were severely disrupted.
Europe (migrants/refugees)	Berger et al. 2021	Imported cases were predominantly concentrated among migrants and refugees originating from diphtheria-endemic countries.



Global analysis	genomic	Hadfield et al. 2022	Multiple distinct <i>C. diphtheriae</i> lineages were identified as circulating globally; outbreak clusters were strongly correlated with areas of suboptimal vaccination coverage.
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The findings demonstrate that diphtheria exhibits a profoundly unequal global distribution, with disease burden disproportionately concentrated in low- and middle-income countries (LMICs), particularly Nigeria, India, and Indonesia (Abbas et al., 2025; Ogunleye et al., 2023; Kamble et al., 2024). These nations continue to face persistent structural challenges including fragmented health systems, inadequate surveillance infrastructure, and incomplete routine immunization programs, all of which facilitate sustained community transmission of *Corynebacterium diphtheriae* (Rahmawati & Wahyuni, 2014; Izza & Soenarnatalina, 2015).

The situation is further exacerbated in humanitarian crisis settings, as evidenced by the massive outbreak affecting over 7,000 individuals in Rohingya refugee camps in Bangladesh (Dureab et al., 2020) and the surge in cases among children in conflict-affected Yemen (Wagner et al.,

2018). These contexts demonstrate how population displacement, overcrowding, and the complete breakdown of essential health services can create optimal conditions for diphtheria transmission and severe outcomes.

In stark contrast, high-income regions such as Europe and North America primarily report sporadic imported cases, typically among unvaccinated migrants and refugees arriving from endemic areas (Berger et al., 2021). This pattern underscores both the effectiveness of sustained vaccination programs in eliminating endemic transmission and the continued vulnerability to importation-related outbreaks. The global genomic analysis further reinforces these geographic disparities, revealing that outbreak clusters consistently emerge in regions with compromised vaccination coverage, regardless of the specific *C. diphtheriae* lineage involved (Hadfield et al., 2022).

Age-Specific Incidence and Mortality Patterns

Table 4. Age-Specific Incidence and Mortality

Age Group	Reference(s)	Observations
Children 2–14 years	Ogunleye et al. 2023; Kamble et al. 2024	This group comprised the majority of confirmed cases across all studies. Case fatality rates reached up to 13%, with unvaccinated children being disproportionately affected.
Adolescents & adults	Edmunds et al. 2019; Hadfield et al. 2022	Rising incidence rates were documented due to waning vaccine-induced immunity. Outbreaks were specifically linked to insufficient booster dose uptake in these populations.
Displaced populations (children <15)	Dureab et al. 2020; Wagner et al. 2018	Children in refugee camps and humanitarian crisis settings faced extreme vulnerability due to complete lack of vaccine access and optimal transmission conditions.

The age distribution of diphtheria cases reveals consistent patterns across diverse geographic and socioeconomic contexts. Children aged 2–14 years consistently bear the greatest disease burden, representing the majority of cases

in every outbreak investigation included in this review (Ogunleye et al., 2023; Kamble et al., 2024). This vulnerability reflects multiple intersecting factors: incomplete primary vaccination schedules, waning



maternal antibody protection after infancy, and increased social mixing in school and community settings.

The case fatality rates among children are particularly concerning, with studies from Nigeria and India documenting rates as high as 13% among hospitalised pediatric cases (Kamble *et al.*, 2024). In the Indian study by Kamble *et al.* (2024), children aged 6–10 years represented the largest proportion of cases, yet only 6.4% had documentation of complete vaccination history, highlighting critical gaps in both vaccination delivery and record-keeping systems. Similarly, Nigerian surveillance data demonstrated that unvaccinated patients had 2.45 times higher odds of mortality compared to fully vaccinated individuals (Abbas *et al.*, 2025).

Perhaps most significantly, emerging evidence from India and global genomic surveillance indicates a troubling epidemiological shift: the increasing incidence of

diphtheria among adolescents and young adults (Edmunds *et al.*, 2019; Hadfield *et al.*, 2022). This phenomenon reflects the natural waning of vaccine-induced immunity over time, combined with inadequate booster immunisation programs in many endemic regions. The implications of this trend are profound, as it suggests that populations previously considered protected may become susceptible to disease, potentially leading to larger and more complex outbreaks.

Children in humanitarian settings represent an extreme manifestation of age-related vulnerability. The Rohingya refugee crisis (Dureab *et al.*, 2020) and Yemen conflict (Wagner *et al.*, 2018) demonstrate how the intersection of young age and humanitarian emergency creates optimal conditions for both disease transmission and severe outcomes, with virtually no access to preventive interventions.

Gender-Specific Differences in Disease Burden

Table 5. Gender-Specific Differences

Gender Pattern	Reference(s)	Findings
Higher male incidence	Kamble <i>et al.</i> 2024; Abbas <i>et al.</i> 2025	Slightly higher incidence rates were observed among males in both surveillance-based and hospital-based datasets from India and Nigeria.
No significant gender difference	Dureab <i>et al.</i> 2020; Edmunds <i>et al.</i> 2019	Several large-scale studies demonstrated near-equal distribution of cases between males and females, suggesting minimal gender-based susceptibility differences.
Gender-related mortality variations	Usamatu <i>et al.</i> 2025	Female patients exhibited higher mortality rates, primarily attributed to delayed healthcare presentation and reduced access to life-saving diphtheria antitoxin treatment.

Gender-specific patterns in diphtheria epidemiology appear considerably less pronounced than the stark age-related differences observed across all studies. The evidence presents a complex picture where biological susceptibility appears relatively equal between sexes, but important disparities emerge in disease outcomes and healthcare access patterns. While some surveillance datasets from Nigeria (Abbas *et al.*, 2025) and hospital records from India (Kamble *et al.*, 2024) suggested marginally higher incidence rates among males, this

pattern was not consistently replicated across all study settings. Large-scale outbreak investigations in refugee populations (Dureab *et al.*, 2020) and multi-country analyses (Edmunds *et al.*, 2019) demonstrated near-equal distribution between genders. The absence of strong gender-based susceptibility differences suggests that *C. diphtheriae* infection risk is primarily determined by vaccination status and exposure opportunities rather than biological sex-related factors.



However, the most concerning finding relates to gender disparities in clinical outcomes and mortality. Hospital-based data from Nigeria revealed significantly higher case fatality rates among female patients, a pattern primarily attributed to delayed healthcare-seeking behaviour and structural barriers in accessing specialised treatment, particularly diphtheria antitoxin (Usamatu et al., 2025). This disparity highlights how socioeconomic and cultural factors can transform equal biological susceptibility into unequal health outcomes. These findings suggest that effective diphtheria control strategies must address not only vaccination coverage gaps but also the underlying social determinants that create barriers to timely healthcare access, particularly for women and girls in resource-constrained settings. The gender-related mortality differences underscore the importance of community education programs that promote early recognition of diphtheria symptoms and immediate healthcare seeking, regardless of patient gender.

Synthesis and Implications

The comprehensive analysis of global diphtheria epidemiology reveals three critical themes that have profound implications for public health policy and practice. First, the pronounced geographic concentration of disease burden in specific LMICs (Abbas et al., 2025; Ogunleye et al., 2023; Rahmawati & Wahyuni, 2014) highlights the urgent need for targeted, sustained interventions to strengthen routine immunisation systems and outbreak response capacity in these regions. Second, the persistent vulnerability of children aged 2–14 years (Kamble et al., 2024; Ogunleye et al., 2023), combined with emerging evidence of waning immunity among adolescents and adults (Edmunds et al., 2019; Hadfield et al., 2022), necessitates a lifecycle approach to diphtheria prevention that extends beyond traditional infant vaccination schedules. This may require fundamental revisions to national immunisation policies in endemic regions. Finally, while gender-based susceptibility differences appear minimal (Dureab et al., 2020; Edmunds et al., 2019), the documented disparities in healthcare access and outcomes (Usamatu et al., 2025) demand gender-sensitive approaches to both prevention and

treatment services. Addressing these inequities will be essential for achieving equitable reductions in diphtheria-related morbidity and mortality across all demographic groups.

Limitations

Several limitations should be considered when interpreting these findings. The geographic distribution of studies may not fully represent global diphtheria epidemiology, with potential underrepresentation of some endemic regions. Variations in surveillance systems and case definitions across studies may affect the comparability of findings. Additionally, the quality and completeness of demographic data varied across studies, potentially influencing the precision of age and gender-specific estimates.

Conclusions

Diphtheria continues to pose a significant public health challenge in specific geographic regions, with distinct demographic patterns that reflect underlying vulnerabilities in health systems and vaccination coverage. The concentration of disease burden among children, the emerging challenges in adolescents and adults, and the persistent gender disparities highlight the need for comprehensive, equity-focused approaches to diphtheria prevention and control. Strengthening routine immunisation systems, ensuring adequate booster coverage, and addressing barriers to healthcare access will be critical to reducing the global burden of this vaccine-preventable disease.

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