Gulf Rapid Risk Assessment: Increase in Diphtheria Cases Globally – Version 2

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This document has been developed by the Gulf Center for Disease Prevention and Control (Gulf CDC) for the awareness of public health authorities within countries of the Gulf Cooperation Council (GCC). The rapid risk assessment provides guidance based on the information available to the Gulf Public Health Emergencies Network as of 31 Jan 2024

I. Background

(a) The Event

The Gulf CDC detected a significant increase in diphtheria cases on 24th of October reported from Nigeria in 2023, making the outbreak the largest historically in the African continent, and the most significant globally with 21,200 cases (12,581 confirmed; 8,619 suspected) and nearly 576 deaths amongst confirmed cases (CFR: 4.6%) up to the epidemiological week 49 of 2023. These cases were reported from 35 of 36 states and the Federal Capital Territory of Nigeria with 77 % of the confirmed cases reported from Kano state of the confirmed cases, only 25% were fully vaccinated (1). Since the detection, the Gulf CDC has been monitoring the Event closely (see figure 1 for the outbreak epicure). As of 18 January 2024, the number of confirmed cases has increased to 13387, with 598 associated deaths (CFR: 4.5%) (2).

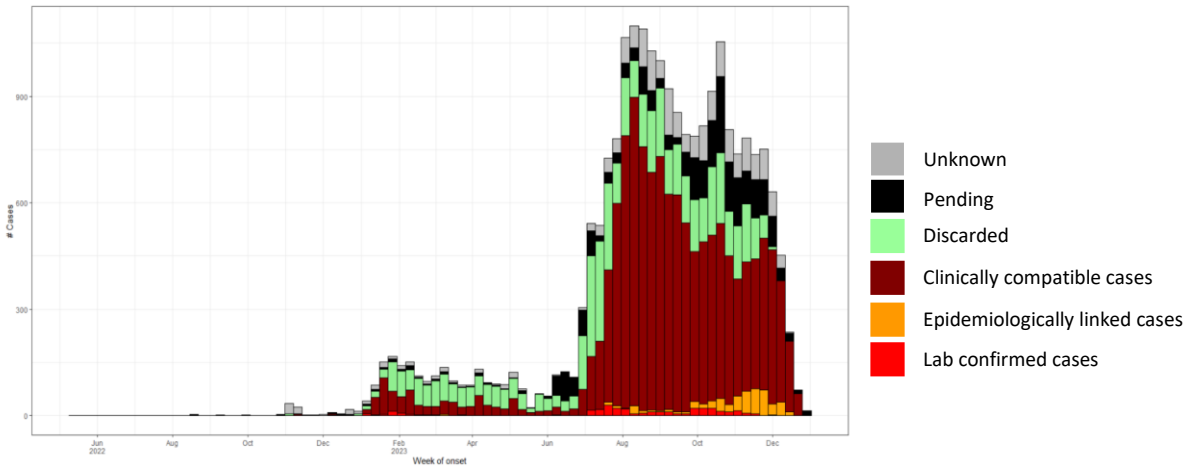

Figure 1. Number of confirmed diphtheria cases by week, Nigeria, May 2022 – Jan 2024, Nigeria Centre for Disease Control and Prevention (2)

In addition to Nigeria, 5 African countries are reporting diphtheria including Algeria, Guinea, Mauritania, Niger, and South Africa. Making the tally of cases in the whole of Africa about 23,120 cases (12,432 confirmed; 10,688 suspected)(1).

Another country that is witnessing a sharp rise in diphtheria cases is Yemen, so far this year, 1671 suspected diphtheria cases with 109 associated deaths have been reported in the country, this is 57% higher than in 2021 and 2022 (3).

Moreover, the Gulf CDC detected on the 19th of November 2023 a report of a continuous increase (since 2022) in imported diphtheria cases among migrants arriving in the United Kingdom. A similar situation is noticed in some European countries including Belgium, Germany, and Switzerland with migrants arriving from endemic countries such as Afghanistan, Syria, and Ethiopia (4). Nevertheless, it is yet unknown if the infection has been introduced into the general population of European and UK citizens.

Furthermore, the Gulf CDC identified diphtheria reports from other countries including the Dominican Republic, Venezuela, Indonesia, Philippines, Vietnam, Pakistan, and India (The detected reports and signals by the Gulf CDC are listed in Annex 1).

This increase in cases has occurred in parallel with a drastic global shortage of diphtheria vaccines and diphtheria antitoxins, due to limited production capacity. The shortage has further

compounded the diphtheria infections, particularly in countries with low vaccination coverage (5).

The Hazard

Diphtheria is mainly caused by diphtheria-toxin-producing *Corynebacterium* species; *Corynebacterium diphtheriae,* and strains of *Corynebacterium ulcerans*. Diphtheria is spread from person to person, usually through respiratory droplets from infected individuals or carriers as well as direct contact with infected individuals or contaminated objects (6).

Symptoms of diphtheria typically appear 2 to 5 days (7 days after skin infection for cutaneous diphtheria) after exposure. Common signs include sore throat, fever, malaise, swollen lymph nodes, lesions appearing as punched-out ulcers, and production of pharyngeal pseudomembranous (tonsils/pharynx that can spread through the upper respiratory tract). Without proper antibiotic treatment, the bacteria will continue to produce toxins that can lead to cardiac (myocarditis, endocarditis, heart failure), renal and neurological (neuropathy, neuritis, motor paralysis) complications. The overall case-fatality rate for diphtheria in not-immunized or under-immunized patients is 3%-16%, with higher death rates (up to 26%) among children younger than 5 years old and people older than 40 years of age (6). The occurrence of the disease in fully vaccinated individuals is very rare (7).
Presumptive diagnosis is based on observation of common signs and symptoms. The diagnosis is confirmed by culture growth of *C. diphtheriae* and identification of toxigenicity by ELEK testing of the lesions or pharyngeal membrane, though treatment should be initiated before confirmation if respiratory diphtheria is suspected.

Administration of diphtheria antitoxin (DAT) for symptomatic patients, antibiotics based on local antibiotic resistance patterns, and supportive care are the main treatment approaches. The diphtheria toxoid, administered as part of the diphtheria-tetanus-pertussis (DTP) vaccine, is the most effective preventive measure against diphtheria, and a universal immunization strategy is the main effective method for preventing the disease spread in communities.

II. Epidemiological Situation

(a) Global

The incidence of respiratory tract diphtheria peaks during colder months (in temperate climates). Historically, tens of thousands of diphtheria deaths were estimated worldwide each year in the late 1990s and early 2000s. However, mortality has declined significantly since 2015 due to widespread vaccination (8).

Asymptomatic carriage rates of C. diphtheriae are estimated to be 3-5% in endemic areas. In 2000, diphtheria accounted for approximately 0.2% of vaccine-preventable deaths among children below the age of 15 globally (9). According to a 2022 systematic review, the global burden was estimated to be around 10,000 cases per year, with 5,300 annual cases in Africa alone (10).

However, resurgences have been documented in multiple countries recently. An estimated 25 million children globally were unvaccinated or under-vaccinated against diphtheria, pertussis, and tetanus in 2021 due to COVID-19 pandemic-related disruptions to immunization programs (11). In Europe, cases have been on the rise since early 2022 associated with the influx of migrants (12), mainly reported by Germany (13).

(b) GCC Countries

Cases of Diphtheria in GCC countries are mainly imported. In 2022-2023, Bahrain, Oman, and Kuwait reported zero cases whereas reports from other GCC countries will be included when they are available.

III. Risk Assessment

(a) RRA Risk Question(s)

What is the risk of a significant number of diphtheria cases being imported into the GCC Region in the upcoming 6 months, in terms of the likelihood and impact of the importation?

(b) Likelihood

The likelihood of diphtheria cases being imported into the GCC countries is **likely.**

There is significant population movement between GCC countries and regions where diphtheria is reported, which poses a risk of imported cases. The possibility of introduction through travelers exists (see Table 1), especially in groups such as expats coming in from high connective countries with low vaccination coverage such as Yemen, which is witnessing a large diphtheria outbreak, this could lead to localized transmission in certain households and communities. It's also important to note that diphtheria is currently not being screened for in the GCC Wafid expatriate screening program, and as such, infected migrants could travel and settle in GCC without being detected.

Furthermore, the upcoming and current mass gathering events, including Riyadh Season, Asian Football Cup in Qatar, Formula One UAE, and COP28. Religious Umra are expected to attract a

significant number of travelers from endemic regions, further increasing the likelihood of imported cases.

Table 1. Probability of an infected case imported to a GCC country with diphtheria in the next 30 days (BlueDot, 2024)

(c) Impact

The impact of diphtheria on the GCC countries is **minor.** Diphtheria is a rare disease in the Gulf Region. Based on data available to the Gulf CDC, immunization coverage estimates for diphtheria, tetanus toxoid, and pertussis (DTP) in 2022 are high but vary across the GCC countries (see table 2). Nevertheless, several upcoming mass gathering events poses a particular risk to increased transmission of diphtheria from the imported cases, particularly in the winter season (as diphtheria peaks globally then).

Table 2. DTP Immunization coverage of citizens and residents in the GCC countries in 2022

Countries of importation risk	United Arab Emirates	Bahrain	Saudi Arabia	Oman	Qatar	Kuwait
Pakistan	15%	1%	15%	1%	2%	0%
Nigeria	1%	1%	16%	0%	1%	1%
United Kingdom	8%	1%	4%	0%	1%	1%
Guinea	2%	0%	1%	0%	0%	0%
Mauritania	0%	0%	0%	0%	0%	0%
Niger	0%	0%	0%	0%	0%	0%

GCC Country	Immunization coverage in 2022*
United Arab Emirates	96.0 %
Bahrain	98.2 %

Saudi Arabia	97.3 %
Oman	99.9 %
Qatar	11349 (number of doses administered at birth, and 4, 6, or 12 months of age)
Kuwait	- 1st dose: 99% - 2nd dose: 94% - 3rd dose: 96% - Booster dose: 99%

*Data is sourced from a survey conducted by Gulf CDC as well as published data from respective Ministry of Health webpages on vaccine services(14–19).

i. *Severity:* The severity of impacts from a diphtheria outbreak in general would vary. Health impacts could be severe, with case fatality rates up to 10% for unvaccinated individuals, with higher death rates (up to 20%) among persons younger than 5 and older than 40 years of age (20). But given the current vaccination coverage in the GCC, the potential severity of diphtheria outbreaks would be low.

ii. *Vulnerability:* Those most vulnerable include young children, the elderly and the immunocompromised due to weaker immune systems. As well as expats, immigrants, or visitors coming in from countries with low vaccination coverage for diphtheria. As long as the vaccination coverage in GCC countries is maintained high, particularly among children, the vulnerability is low.

iii. *Coping capacities:* The response capacity for diphtheria in GCC countries is generally advanced. Despite the global shortage, countries such as Saudi Arabia have secured sufficient antitoxins and vaccines. Some GCC countries, Bahrain, Oman and Kuwait, have begun the administration of diphtheria booster vaccines as per national recommendations (for example Oman and Kuwait are providing TDAP/DTP booster doses to 2-4 years of age, adolescents, and specifically in Oman, pregnant women are also given booster doses *w*hereas in Kuwait, booster doses of the vaccine are also given at the age of 10-12 and 16-18 years.

(b) Level of Confidence

The level of confidence in the assessment is **satisfactory**. The available data provides a reasonable basis for the assessment, but there is some uncertainty due to lack of information on the status of immunization of expat migrants.

(c) Overall Risk level and statement

Risk assessed					
Negligible	Very Low	Low	Moderate	High	Extreme
Based on the available data at this point of time, within the next 6 months, the overall risk of diphtheria case importation in the GCC countries is assessed as low.					
The probability of diphtheria importation in the GCC countries is likely and is driven by increased travel from endemic regions and countries reporting increasing transmission (particularly for mass gathering events). There is a satisfactory level of confidence due to available data on vaccination rates and travel information, though uncertainties remain around the potential for undetected imported cases. The magnitude of the impact of diphtheria case importation into the GCC on the general population is minor, driven by high vaccination coverage, high infection prevention and control measures and availability of diagnostic kits, antitoxins and vaccines.					

V. Recommendations

The GCC countries should consider the following recommended actions for guiding national strategies and strengthening capacities:

1. Ensure readiness (equipment and consumables) for early case confirmation of cases of antibiotic resistance.
2. Training of frontline health workers in the GCC for a high index of suspected cases.
3. Identify isolation areas in hospitals (COVID-19 style isolation); while ensuring staff and equipment are available to manage complications of cases.
4. Training and equipping hospitals for early laboratory confirmation of diphtheria by culture, PCR, ELEK testing, genomic sequencing of isolates, and identifying antibiotic resistance patterns.
5. Raise awareness among healthcare professionals about the current global diphtheria situation, in addition to developments regarding the emergence of antibiotic resistance, and the possible effects of the global vaccine shortage. This is particularly important for ensuring detection, as diphtheria may not be commonly suspected in the GCC due to its limited incidence and high national vaccination rates.
6. Raise awareness of travel clinics and encourage informing travelers to regions experiencing diphtheria outbreaks to ensure they receive the necessary vaccinations or a booster dose based on national regulations.
7. Evaluate the feasibility and usefulness of checking the diphtheria vaccination status in centers registered with the GCC Wafid program in countries reporting high transmission of diphtheria. This will support identification of migrants that require a DTAP booster vaccination and will ultimately support maintaining the high immunization rates across the GCC, reducing the risk of spread. (**This recommendation shall be evaluated further by relevant Gulf committees.**)_
8. Consider evaluating a recommendation for diphtheria booster vaccine dose prior to entry into GCC, for travelers from affected countries.

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Annex 1. Signals of unusual increase in diphtheria cases globally detected by the Gulf CDC (November 2022 – November 2023)

Detection Date	Location	Cases and deaths (If applicable)
19/11/2022	Pakistan	39 deaths
27/11/2022	UK	50 cases and 1 death
02/12/2022	Europe	231 cases
13/02/2023	Nigeria	38 deaths
13/02/2023	Dominican Republic	4 cases and 1 death
07/03/2023	Nigeria	Significant increase in cases
14/03/2023	Venezuela	3 cases
21/03/2023	Indonesia	14 deaths
10/04/2023	Philippines	20 cases
09/07/2023	Nigeria	798 cases
01/08/2023	Nigeria	2,455 cases and 83 deaths
13/08/2023	Algeria	80 cases
07/09/2023	Viet Nam	1 death
20/09/2023	Nigeria	9,000 cases and 307 deaths
22/10/2023	Guinea	538 cases and 58 deaths
24/10/2023	Nigeria	14,000 cases
25/10/2023	India	3 cases and 3 deaths
20/11/2023	Pakistan	259 cases
21/11/2023	United Kingdom	83 cases
18/12/2023	United Kingdom	1 case
21/12/2023	Pakistan	Rapid increase in pediatric patients
26/12/2023	Nigeria	20104 cases and 573 deaths
03/01/2024	Ukraine	1 death

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