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Diphtheria outbreak and associated risk factors assessment in Khyber Pakhtunkhwa, Pakistan

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Abstract

Diphtheria, a highly infectious disease that may be prevented by vaccine, is spreading and poses a serious threat of becoming an epidemic and major public health concern in Khyber Pakhtunkhwa, Pakistan. This study was aimed to examine the epidemic from an epidemiological standpoint and offer management recommendations in Khyber Pakhtunkhwa during the year 2024. Data of Diphtheria cases were collected from Districts Health Information System (DHIS) of Health Department Khyber Pakhtukhwa for the year 2024 reported from 28 districts of the province. The data revealed 683 confirmed cases of diphtheria across 28 districts, underlining the significant public health issue faced by the disease's ability to spread rapidly. Among these, 58 cases were verified by laboratory testing, highlighting the critical need for improved diagnostic services to detect diphtheria rapidly and reliably. The study identifies six distinct outbreaks verified in laboratories in Peshawar Nowshera, Charsadda, Bannu, Mardan, and Swat, demonstrating the disease's widespread geographic reach and the need for focused public health interventions in these locations. A higher prevalence was identified in those over the age of five (87%). There is a substantial opportunity to reduce and ultimately extinguish the risk of diphtheria becoming an uncontrolled epidemic in the region by implementing a comprehensive and multifaceted approach.

Introduction

Diphtheria is caused by the Gram-positive Rod C. diphtheriae and is distinguished by laryngitis, pharyngitis, or tonsillitis in the presence of an adhering membrane in the tonsils, throat, and/or nose (WHO, 2003). Up to 25% of patients develop myocarditis, and the condition can also impact the peripheral nervous system, resulting in temporary paralysis (MacGregor et al., 2009). *C. diphtheriae's* pathogenicity is caused by an extracellular toxin, and those with inadequate immunization or insufficient antitoxin antibody levels are more vulnerable to infection (WHO, 2006). Diphtheria is treated with antitoxin and either penicillin or erythromycin, while DAT is not currently widely available in Nigeria (Sadoh and Sadoh, 2011).

The advent of the diphtheria vaccination in the early twentieth century, notably the diphtheria-tetanus-pertussis (DTP) vaccine, greatly lowered the disease's occurrence (Rappuoli

and Malito , 2014) This historical backdrop highlights the long-standing difficulty of diphtheria as a public health concern, which evolved from ancient descriptions to more thorough understandings in succeeding decades. Diphtheria's history demonstrates the enormous influence of modern advances in infectious diseases and immunology, which have transformed it from a fearsome sickness to a preventable condition. Although diphtheria is well controlled in many parts of the globe because to extensive immunization, it remains a hazard, particularly in places with insufficient vaccine coverage (Truelove *et al*., 2020). Diphtheria is a highly infectious, vaccine-preventable disease. The illness is lethal in 5-10% of instances, with a greater fatality rate in small children. In areas with limited availability to diphtheria antitoxin, the crude fatality rate (CFR) can reach 40% (Oduove *et al*., 2024).

Despite vaccine availability, diphtheria outbreaks continue in impoverished nations. The World Health Organization (WHO) reported its most recent epidemic in Guinea in October 2023. A deadly diphtheria outbreak occurred in Guinea's Kankan area between July 4 and October 13, 2023. The overall number of reported cases was 538, including 520 suspected and 18 laboratory-confirmed cases of the illness. This epidemic resulted in 58 deaths, with 13 among the confirmed cases. This resulted in an overall case fatality rate (CFR) of 11% across all reported cases (Zwizwai, 2023).

Notably, the demographic group most impacted by this outbreak was children aged 1-4, accounting for the majority of infections. Recently, an outbreak of diphtheria has occurred in one of the world's most violent regions, Khyber-Pakhtunkhwa, Pakistan, and there is a possibility of an epidemic as the Pakistani government makes all efforts to return Afghan refugees to Afghanistan. This risk is worsened by the Pakistani government's continued efforts to return Afghan refugees to Afghanistan, which might further destabilize the already vulnerable public health situation Yousaf, 2020).

In this regard, the purpose of this study was to conduct an epidemiological assessment of the situation and make recommendations for how to address it. The evaluation research considers a variety of parameters, including the demographic and geographic distribution of cases, the incidence of infection, and the efficacy of current public health interventions. It also examines the influence of refugee migrations on disease transmission and identifies high-risk communities that need rapid treatment. The outcomes of this study are critical for guiding public health policies and interventions. Recommendations are made to effectively address the situation, focusing on both short-term emergency remedies and long-term prevention measures. The study also investigates the possibility of international collaboration and aid, as the pandemic has far-reaching consequences.

Materials and Methods

Study Area

Khyber Pakhtunkhwa, located in northwest Pakistan, is one of the country's four administrative provinces, despite its tiny size. It has seven divisions and 36 districts. According to the most recent census estimates, the province's population increased from 17.7 million to 30.5 million between 1998 and 2017, above Pakistan's overall growth rate of 2.40% by 2.89% (Wazir and Goujrn, 2021) Predominantly rural, 81% of the population lives in the countryside,14 despite the presence of some heavily populated towns, like Peshawar, which has 2.1 million people. Furthermore, it is anticipated that more than 3 million Afghan refugees have arrived in the area (Braam, 2022).

Khyber Pakhtunkhwa has seen years of assault and political uncertainty, posing enormous economic and social development hurdles. The surge of refugees, continued conflict, and prolonged instability have all had a negative impact on the region's economy (Baloch et al., 2017).

Ethical Statement

Since the study's data contained no patient identifying information, the ethical board does not need to fully evaluate it. Before the study started, all required consents and permissions were acquired from the data holders.

Study Design

This study used a retrospective approach to determine the prevalence and incidence rates of diphtheria in Khyber Pakhtunkhwa (KPK), Pakistan. The study sought to offer a thorough assessment of the disease's impact over a certain time period by analyzing historical data from medical records, health surveys, and regional health department reports. The retrospective study method entailed methodically evaluating patient records from hospitals and clinics throughout KPK, finding verified cases of diphtheria, and collecting pertinent information such as patient demographics, clinical features, and outcomes.

This technique allowed the researchers to compute the prevalence rate, which reflects the proportion of the population afflicted by diphtheria at a certain moment in time, as well as the incidence rate, which quantifies the number of new cases occurring during a given time period. In addition to frequency and incidence rates, the study aimed to uncover possible risk factors for diphtheria infection. This involved investigating characteristics such as age, gender, socioeconomic position, immunization history, and geographic region. Understanding these risk variables is critical for designing effective public health interventions and disease prevention methods.

Furthermore, the retrospective research design enabled the analysis of temporal patterns in diphtheria cases, offering insights into how the illness has evolved in KPK. This data is critical for assessing the efficacy of previous and current public health interventions and identifying areas where greater efforts are required. The study's goal is to highlight the regional burden of diphtheria by accurately estimating prevalence and incidence rates, as well as the

urgent need for improved surveillance, vaccination campaigns, and health-care infrastructure improvements to mitigate the impact of this potentially fatal disease.

Results

Diphtheria is a substantial public health hazard in Khyber Pakhtunkhwa, Pakistan, as indicated by data gathered until December 2024. A total of 683 diphtheria cases have been documented in 28 districts and 325 Union Councils (UCs), demonstrating the spread of this bacterial illness. The study identified six unique outbreaks, which were verified by lab testing, in the districts of Peshawar (208/683, 30.45%), Nowshera (88/683, 12.88%), Charsadda (65/683, 9.51%), Bannu (53/683, 7.75%), Mardan (47/683, 6.88%), and Swat (31/683, 4.53%). (**Table 1a & Figure 1b**)

These incidents highlight the disease's diverse geographical distribution and the importance of focused public health interventions throughout the province. This widespread geographic distribution demonstrates the disease's propensity to afflict both urban and rural people, emphasizing the critical need for a strong public health response. The issue is aggravated by the presence of 58 laboratory-confirmed outbreaks, which indicate localized clusters of illness that might possibly spread to larger epidemics if early measures are not implemented.

Table 1a: Showing district wise detail of Diphtheria cases in Khyber Pakhtunkwha, Pakistan

S. No	District	NO. of cases	Percentage
1	Peshawar	208	30.45 %
2	Nowshera	88	12.88 %
3	Charsadda	65	9.51 %
4	Bannu	53	7.75 %
5	Mardan	47	6.88 %
6	Swat	31	4.53 %

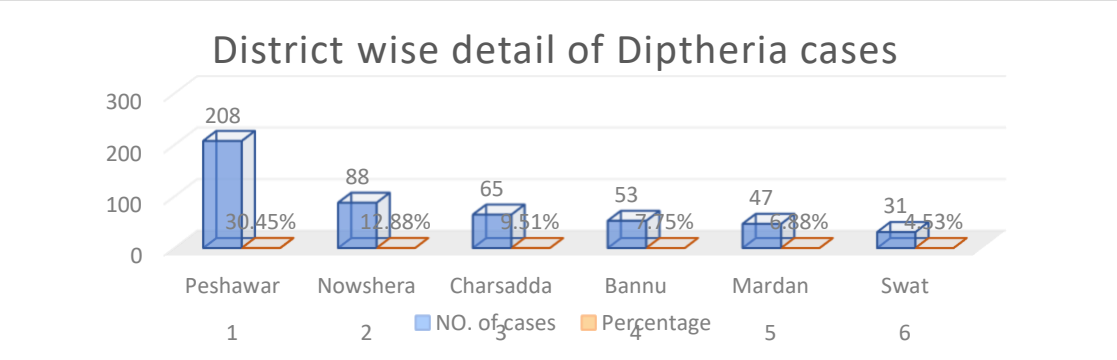

Figure 1b : Showing district wise detail of Diphtheria cases in Khyber Pakhtunkwha, Pakistan

One of the most concerning characteristics of this outbreak is the vaccination status of the afflicted people. A staggering 92% of the reported cases (n=625) were people who had no recorded history of taking the diphtheria, pertussis, and tetanus (DPT) vaccination. This significant figure emphasizes the importance of insufficient immunization coverage as a primary cause of the current pandemic. Despite the global effectiveness of immunization efforts in lowering diphtheria incidence, this data shows considerable gaps in vaccine uptake, which might be attributed to logistical problems, vaccine hesitation, or systemic inadequacies in the healthcare delivery system. This situation emphasizes the importance of prioritizing routine immunization programs while also addressing challenges to vaccine accessibility and uptake.

The age distribution of the patients exacerbates the problem. A considerable 87% (n=592) of the cases are recorded in people aged five years or older, with ages ranging from 60 months to 42 years (**Table 2a and Figure 2b**). This vast age range implies that diphtheria is not limited to young children, who are commonly regarded as the major target population for DPT vaccine. Instead, it exposes weaknesses in older age groups, which might indicate a lack of booster doses or diminishing immunity over time. The presence of people as elderly as 42 years old in the afflicted population suggests a probable cohort effect, in which specific age groups missed vaccinations during previous immunization campaigns or periods of political or social turmoil.

Table 2a: Showing age wise detail of Diphtheria cases in Khyber Pakhtunkwha, Pakistan

S. NO	Age group	NO. of cases	Percentage
1	<5 years	91	13 %
2	≥5 years	592	87 %

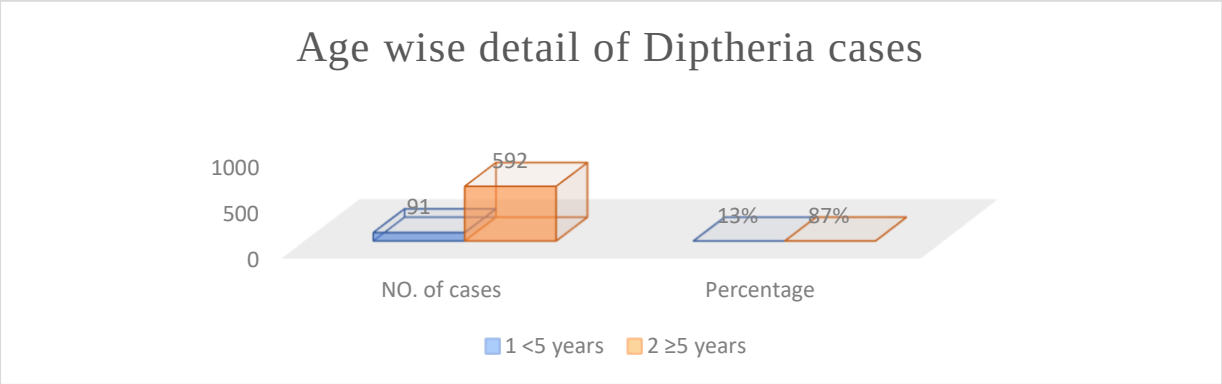

Figure 2b: Showing age wise detail of Diphtheria cases in Khyber Pakhtunkwha, Pakistan

The mortality numbers highlight the outbreak's severity. 31 diphtheria-related deaths have been documented, resulting in a case fatality rate (CFR) of around 4.5% in 2024. While this CFR is consistent with worldwide estimates for treated patients, it serves as a sharp reminder of diphtheria's potentially lethal nature, especially when prompt availability to antitoxin and supportive treatment is restricted. The deadly consequences underline the necessity of early detection, fast response mechanisms, and the availability of life-saving medications in hospital settings.

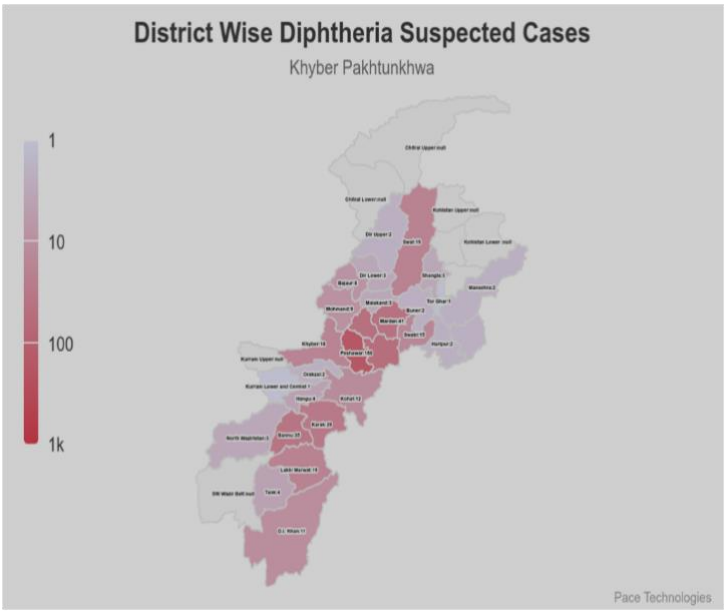

Figure 3: A choropleth map showing diphtheria cases in various districts.
(EPI Review, 2024)

The present diphtheria outbreak demonstrates the essential relationship between vaccination coverage, age-related vulnerabilities, and healthcare system preparation. The significant number of unvaccinated people and the diverse age range of afflicted patients

highlight the importance of a comprehensive public health plan. To reduce diphtheria transmission and avoid future outbreaks, regular immunization programs must be strengthened, booster doses made available, and disease surveillance improved. Addressing the underlying reasons of vaccine hesitancy and raising community understanding about the advantages of immunization will also be critical in reducing this avoidable disease.

Discussion

The present study identifies major obstacles in controlling infectious and non-infectious diseases in low-resource settings like Khyber Pakhtunkhwa, Pakistan. Delayed case identification is a widespread problem, especially for illnesses with symptoms similar to tonsillitis, where people frequently seek medical attention at late stages (Eiseberg et al., 2021). This delay raises the risk of misdiagnosis, contributes to greater transmission rates, and diminishes the proportion of laboratory-confirmed cases. As a result, illness development becomes more difficult, emphasizing the importance of quick and precise diagnosis (Eiseberg *et al.,* 2021; Gunning *et al*., 2020; Sein *et al*., 2016).

Inappropriate responses to disease outbreaks, such as diphtheria, may include focused efforts in the local or neighboring areas, resulting in ineffective disease control. Vaccination coverage remains a major problem, particularly among youngsters who have not gotten any doses or have finished the whole schedule. Compliance with second-dose immunizations is frequently challenging, particularly among adults. The prevalence of diphtheria infections in people aged five and up calls into question long-held beliefs that the disease affects only young children. This conclusion emphasizes the need to revise vaccination campaign target groups and the relevance of community-wide immunity in protecting all ages (Siegel et al., 2018).The diverse age range of those afflicted, ranging from babies to the elderly, emphasizes the general sensitivity to diphtheria in the absence of appropriate immunization, demanding universal coverage rather than focusing primarily on pediatric groups.

The case fatality rate (CFR) of 5%, which equates to 16 fatalities, highlights the seriousness of diphtheria and its preventability with efficient immunization efforts. School-age children were identified as the most afflicted population, indicating the possibility of fast disease spread within and between communities. Even vaccinated youngsters who have not had booster doses remain susceptible to illness. Because of its scarcity, anti-diphtheria serum (ADS) is difficult to get. Furthermore, antibiotic distribution is hampered by resistance, which is frequently caused by financial barriers and the absence of symptoms in asymptomatic carriers, complicating attempts to prevent disease transmission. Limited district-level resources for free antibiotics worsen the issue by extending infectious periods and increasing transmission risks.

The provision of prophylactic antibiotics for close contacts of confirmed patients is critical for limiting transmission and preventing the emergence of asymptomatic carriers (Truelove et al., 2020). Implementing successful control measures requires coordinated efforts from public health authorities, healthcare providers, and the community. Public awareness

efforts must highlight the significance of timely immunization and early treatment seeking behavior. Collaboration with international health organizations can offer the technical and financial assistance needed to boost diphtheria control efforts in the region (Pagliusi *et al.,* 2019). The persistent threat of vaccine-preventable illnesses in Khyber Pakhtunkhwa emphasizes the importance of monitoring and aggressive public health initiatives.

The terrible loss of 16 lives due to a preventable illness highlights the importance of improving public health measures. Strategies to strengthen vaccine supply chains, raise immunization awareness, and extend outreach initiatives to underprivileged populations are critical for reducing the danger of future outbreaks. Diphtheria-Pertussis-Tetanus (DPT) vaccine coverage is poor, indicating systemic inadequacies in public health infrastructure and outreach initiatives. Factors such as vaccination accessibility, population awareness, and vaccine reluctance all contribute to this disparity, emphasizing the need for focused treatments.

Continuous surveillance and study are required to better understand the dynamics of vaccine-preventable illnesses across populations and geographies. Such initiatives can help to uncover immunization gaps, understand disease transmission patterns, and develop targeted therapies to meet the requirements of certain communities. Public health officials must actively combat vaccine misinformation, which contributes considerably to vaccine reluctance and low immunization rates. Delays in getting specialized healthcare services not only jeopardize patient outcomes, but also promote disease spread. Furthermore, insufficient infection prevention and control (IPC) procedures in healthcare settings turn hospitals into potential hotspots for diphtheria transmission.

The delayed speed of on-the-ground investigations and response operations exacerbates the disease's spread in impacted areas. Finally, the absence of preventive antibiotics for close contacts is a wasted chance to break the transmission chain successfully. To address these issues, a diversified strategy is required, including better public health infrastructure, improved vaccination distribution systems, extensive community participation, and long-term international partnership. These activities are critical for averting future epidemics and protecting public health in susceptible places.

Conclusion

The findings highlight the importance of a comprehensive approach to address the recurrence of diphtheria in Khyber Pakhtunkhwa. A multifaceted strategy, as advised, is critical for strengthening the region's ability to successfully prevent and control diphtheria epidemics. Each recommended proposal is crucial to an overall diphtheria control strategy. Increasing immunization coverage is critical. Adding booster doses to the Expanded Programme on Immunization (EPI) schedule closes a crucial gap in the present immunization approach. This strategy would assist to sustain population immunity while also protecting against the

possibility of immunity decreasing over time. Targeting all age groups, with an emphasis on the most vulnerable demographics, is critical to ensuring broad coverage. Another essential proposal is to improve diagnostic and laboratory capacity. Controlling an outbreak requires quickly and properly identifying diphtheria cases. Improved laboratory capacity ensures rapid diagnosis, allowing health officials to conduct targeted treatments quickly. This includes teaching health care personnel to recognize diphtheria signs and properly manage cases, which is critical for early diagnosis and containment.

Conflict of Interest: The authors declare no conflict of interest

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