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CLINICO–Demographic Profile and Outcomes of Hospitalised Children With Diphtheria in A Tertiary Care Hospital of Peshawar

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ABSTRACT

Aim: To determine the clinico-demographic profile and predictors of mortality in hospitalised children with diphtheria.

Methods: This retrospective cohort study included 202 children aged 5–16 years diagnosed with diphtheria per WHO criteria at Lady Reading Hospital, Peshawar, from January 2023 to December 2024. Data on demographics, vaccination status, clinical features, complications, antibiotic use and outcomes were collected from HMIS records and treatment charts. Multivariable logistic regression was used to identify independent predictors of in-hospital mortality.

Results: Mean age was 8.44 ± 2.69 years; 52.5% were male and 64.9% unvaccinated. Fever (96.0%), cough (93.1%) and throat pain (85.2%) were the most common presentations. Complications included airway obstruction (15.8%), respiratory failure (14.9%) and carditis (14.4%). Linezolid, alone or in combination, was the most frequently used antibiotic (59.4%). The case fatality rate was 15.8%. In multivariable analysis, carditis was the only independent predictor of mortality (adjusted OR 18.50; 95% CI 4.72–88.92; $p < 0.001$); antibiotic choice and vaccination status were not significantly associated with death.

Conclusion: Mortality in children hospitalised with diphtheria remains substantial, with carditis as the strongest independent predictor of death. The high case fatality rate, predominantly among unvaccinated children, highlights the need for early cardiac evaluation and strengthened vaccination programmes.

1 | Introduction

Diphtheria is a bacterial infection caused by *Corynebacterium diphtheriae*. This infection infiltrates the mucous membranes of the throat, resulting in the production of a diphtheria toxin that disrupts protein synthesis and ultimately leads to cell death [1]. Though this disease is eliminated from developed countries, it is still endemic in some Asian countries like India and Pakistan [2]. Despite the availability of preventive measures such as vaccination, diphtheria persists as a substantial public health challenge in these regions. Diphtheria is clinically distinguished by the formation of a characteristic membranous growth in the throat, causing respiratory blockage, and it is often associated with severe complications like myocarditis and neurological sequelae [3]. The outcomes of diphtheria in children are influenced by multiple factors

Abbreviations: CFR, case fatality rate; CI, confidence interval; CK-MB, creatine kinase-myocardial band; DPT, diphtheria-pertussis-tetanus (vaccine); DTP3, third dose of diphtheria-tetanus-pertussis vaccine; ECG, electrocardiogram; HMIS, Health Management Information System; IQR, interquartile range; IRB, institutional review board; LAMA, left against medical advice; LRH, lady reading hospital; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; SD, standard deviation; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

Summary

- Diphtheria still causes significant child deaths in Pakistan, yet data on what drives mortality in hospitalised children from this region are scarce.
- Among 202 children admitted with diphtheria, carditis was the only independent predictor of death, with an adjusted odds ratio of 18.50, and the overall case fatality rate was 15.8%.
- Early cardiac monitoring in all diphtheria cases and better vaccination coverage, especially in children who missed their booster doses, are key to reducing deaths.

including the timeliness of diagnosis, vaccination coverage and the prompt administration of appropriate therapeutic interventions [4].

As per a report released by the National Institutes of Health (NIH), there has been a notable escalation in the incidence of sporadic diphtheria cases within Pakistan [5]. By December 2022, it was reported that 39 children and teenagers had succumbed to the disease, a number that increased to over 45 by January 2023 [5]. Regarding the trend of vaccination, in 2020, the United Nations Children's Fund (UNICEF) highlighted a 7% drop in childhood vaccination rates in Pakistan, increasing the number of unprotected children to 1.4 million [6]. The true extent of existing cases remains uncertain, primarily attributed to the limitations of the country's healthcare infrastructure.

Globally, the disease carries a case fatality rate (CFR) of around 5%–10%, and this can rise to 20% in young children and older adults. If left untreated, the mortality rate may reach as high as 30%–40% [7]. Due to immunisation programs, the global burden of diphtheria has dropped significantly, but the disease continues to re-emerge in areas where vaccine coverage is low or inconsistent [8]. Although Pakistan's Expanded Programme on Immunization has made progress, DTP3 coverage still hovers around 85%, and booster doses are not routinely given (UNICEF) [9]. This leaves many older children vulnerable to infection. Several factors contribute to diphtheria-related deaths. These include incomplete or missed vaccinations, delayed diagnosis and hospital presentation, limited access to diphtheria antitoxin and complications like myocarditis, respiratory failure and airway obstruction. Socioeconomic challenges such as poverty, lack of awareness and healthcare access barriers further compound the risk [10, 11].

In light of the persistent admissions of diphtheria in various tertiary care hospitals, this research endeavours to contribute to the body of knowledge that can guide healthcare professionals, policymakers and public health authorities in the development of effective strategies to reduce the burden of diphtheria, improve vaccination campaigns and enhance the management of diphtheria cases. The aim of this research is to comprehensively examine the clinico-demographic profile and outcomes of hospitalized children with diphtheria in Peshawar, shedding light on the current epidemiological trends and challenges faced in managing this infectious disease in the region.

The objective of this study was to determine the clinic-demographic profile and predictors for mortality of hospitalised children with diphtheria.

2 | Materials and Methods

This retrospective cohort study was conducted at the Paediatric department, Lady Reading Hospital (LRH), Peshawar from 1st January 2023 till 31st December 2024.

The required sample size was calculated using OpenEpi, based on a reported mortality rate of 8.6% among diphtheria-affected children [12]. With a 95% confidence level and a 5% margin of error, the estimated sample size was $n = 121$. However, to increase the statistical power of the study, we included all available data, comprising a total of 202 patients.

Data from all diphtheria patients (as defined by the operational criteria) between January 2023 and December 2024 were collected from the Health Management Information System (HMIS) and treatment charts using a non-probability consecutive sampling technique. Informed consent was not required for this study, as consent for the use of anonymised data in research had already been obtained from patients' parents or guardians as part of their treatment process.

The inclusion criteria comprised all patients diagnosed with diphtheria, according to the operational definition, who were admitted to the paediatric unit of LRH, regardless of gender or ethnicity, and aged between 5 and 16 years. Patients were excluded if they were younger than 5 years or older than 16 years, had a known diagnosis of structural heart disease, presented with an alternative diagnosis such as other causes of membranous tonsillitis or had conditions such as bronchiectasis, cystic fibrosis or known tuberculosis. Additionally, patients who absconded, left against medical advice (LAMA) or had incomplete data were also excluded from the study.

After approval of the study synopsis by the Institutional Review Board (IRB) of LRH, data were retrieved from the HMIS and treatment charts of all patients diagnosed with diphtheria, according to the operational definition. Diphtheria was defined as per the World Health Organization (WHO) criteria: "an illness of the upper respiratory tract characterized by pharyngitis, nasopharyngitis, tonsillitis or laryngitis, and a firmly adherent greyish-white, thick patchy to confluent membrane, which bleeds on dislodgement." Information was collected using a structured proforma and included demographic details (age and gender), clinical presentation, immunization status, history of contact with a known diphtheria case, site and extent of the pseudomembrane, complications, laboratory and microbiological findings, treatment details and outcomes. Antibiotic use was categorised as Benzyl Penicillin, Ceftriaxone, Ceftriaxone with other antibiotics, Linezolid, Linezolid with other antibiotics and Meropenem with Ceftriaxone. Vaccination status was classified as follows: *Completely immunised*—children who had received three

primary doses of the diphtheria–pertussis–tetanus (DPT) vaccine starting at 6 weeks of age, followed by booster doses at 16–24 months and 5–6 years; *Partially immunised*—those who had missed one or more of the primary or booster doses; and *Unimmunised*—those who had not received any dose of DPT or booster or were unaware of their immunisation status. Hospital stays and the duration of illness before admission were recorded in days as mean ± standard deviation (SD). Clinical features such as fever, cough, throat pain and difficulty in breathing were documented. Complications were carefully recorded based on clinical, radiological and laboratory findings. Carditis was identified based on clinical signs (tachycardia disproportionate to fever, gallop rhythm, hypotension), electrocardiogram changes and elevated cardiac biomarkers such as troponin or CK-MB. Airway obstruction was recorded in cases requiring urgent airway management, including use of oxygen therapy, nebulisation or endotracheal intubation, based on signs of stridor, use of accessory respiratory muscles or low oxygen saturation. Respiratory failure was defined as the need for ventilatory support due to inadequate oxygenation or ventilation, confirmed by arterial blood gas analysis and clinical deterioration. Laryngeal membrane formation was noted upon direct visualisation during laryngoscopic examination or inferred from characteristic upper airway symptoms in conjunction with imaging. The outcome variable focused on mortality, recorded based on the patient's clinical course during hospitalisation. All patients received antidiphtheria toxin as part of their initial treatment regimen.

Data was analysed using R software version 4.3.2. Continuous variables were summarised as mean ± SD or median with interquartile range (IQR) and categorical variables as frequencies and percentages. Variables with normal distribution are presented as mean ± SD, while skewed variables are presented as median (IQR). Hospital length of stay was found to be non-normally distributed and is therefore reported as median (IQR). Comparisons by mortality status were performed using the Wilcoxon rank-sum test for continuous variables and the Chi-square or Fisher's exact test for categorical variables. Logistic regression analysis was conducted to identify independent predictors of mortality, with mortality as the dependent variable. Results were reported as adjusted odds ratios (ORs) with 95% confidence intervals (CIs), and a p-value < 0.05 was considered statistically significant.

3 | Results

A total of 202 diphtheria cases were analysed. The mean age was 8.44 years (SD ± 2.69), with slightly more males (52.5%, $n = 106$). Most patients were unvaccinated (64.9%, $n = 131$), and 20.8% ($n = 42$) were partially vaccinated. Linezolid, either alone or in combination, was the most commonly administered antibiotic (59.4%, $n = 120$). Benzyl penicillin was used in 26.7% ($n = 54$), and ceftriaxone alone or with other drugs in 10.9% ($n = 22$). Meropenem with ceftriaxone was rarely used (3.0%, $n = 6$). The mean hospital stay was 4.79 days (SD ± 4.73), and symptoms had been present for an average of 5.35 days (SD ± 1.73) before admission. Fever (96.0%, $n = 194$), cough (93.1%, $n = 188$) and throat pain (85.2%, $n = 172$) were the most common symptoms; 33.7% ($n = 68$) had difficulty breathing. Complications included airway obstruction (15.8%, $n = 32$), respiratory failure (14.9%, $n = 30$) and carditis (14.4%, $n = 28$). The CFR was 15.8% ($n = 32$) (Table 1).

Among the 202 diphtheria cases, 32 patients (15.8%) died. Median age did not differ significantly between survivors and non-survivors (8.00 years in both groups; $p = 0.7$). Mortality was significantly higher in males (75.0%, $n = 24$) compared to females (25.0%, $n = 8$; $p = 0.005$). Antibiotic regimen was associated with outcome ($p = 0.005$), with higher mortality seen in those receiving linezolid (25.0%, $n = 8$) or its combinations (56.3%, $n = 18$). In contrast, only 6.3% ($n = 2$) of those who died had received benzyl penicillin. Vaccination status showed no significant association with mortality ($p = 0.12$), although the majority of deaths occurred in unvaccinated individuals (81.3%, $n = 26$). Median hospital stay was shorter in those who died (3.0 days vs. 4.0 days; $p = 0.016$), while duration of illness prior to admission was similar ($p = 0.14$). It is important to note that the shorter median hospital stay among non-survivors (3 days) compared to survivors (4 days) reflects early in-hospital death rather than any protective effect of prolonged admission, as the majority of deaths occurred within the first 3 days of admission, consistent with rapid disease progression. Clinical features such as throat pain ($p = 0.006$), difficulty in breathing ($p < 0.001$), carditis ($p < 0.001$), airway obstruction ($p < 0.001$), respiratory failure ($p < 0.001$) and laryngeal membrane formation ($p = 0.002$) were significantly more frequent among non-survivors. Fever and cough were common across both groups without significant differences (Table 2). No neurological complications, including peripheral motor neuropathy or palatal palsy, were documented during the inpatient stay.

In multivariate logistic regression, carditis emerged as the only independent predictor of mortality in diphtheria cases. Patients with carditis had significantly higher odds of death (adjusted OR 18.50, 95% CI 4.72 to 88.92; $p < 0.001$) compared to those without. While male sex was significantly associated with mortality in univariable analysis (OR 3.22, 95% CI 1.42 to 8.02; $p = 0.007$), this association was not sustained after adjustment (adjusted OR 1.42, 95% CI 0.45 to 4.55; $p = 0.548$). Similarly, difficulty in breathing (adjusted OR 0.77, $p = 0.773$) and presence of a laryngeal membrane (adjusted OR 1.15, $p = 0.920$) did not remain significant after controlling for other variables. Antibiotic choice did not significantly impact mortality in the adjusted model. Compared with ceftriaxone, neither linezolid (adjusted OR 0.73, $p = 0.738$) nor penicillin (adjusted OR 0.29, $p = 0.292$) showed a statistically significant association with reduced odds of death (Table 3).

4 | Discussion

Our study shows that diphtheria primarily affects unvaccinated school-aged children, with a slight male predominance. Most children presented with common respiratory symptoms such as fever, cough and throat pain, while a notable proportion developed severe complications, including airway obstruction, respiratory failure and carditis. Although several clinical features and male sex were associated with higher mortality in univariable analysis, only carditis emerged as an independent predictor of death in multivariate analysis. While linezolid was

TABLE 1 | Demographic characteristics, clinical features and outcomes of diphtheria cases ($N = 202$).

Variable	Category	n (%) / Mean (SD)	95% CI
Age (years)	—	8.44 (2.69)	8.07–8.81
Gender	Female	96 (47.52)	40.47–54.65
	Male	106 (52.48)	45.35–59.53
Vaccination status	Partially vaccinated	42 (20.79)	15.42–27.05
	Unvaccinated	131 (64.85)	57.84–71.42
	Vaccinated	29 (14.36)	9.83–19.96
Fever	No	8 (3.96)	1.73–7.65
	Yes	194 (96.04)	92.35–98.27
Cough	No	14 (6.93)	3.84–11.36
	Yes	188 (93.07)	88.64–96.16
Throat pain	No	30 (14.85)	10.25–20.52
	Yes	172 (85.15)	79.48–89.75
Difficulty breathing	No	134 (66.34)	59.37–72.82
	Yes	68 (33.66)	27.18–40.63
Carditis	No	154 (86.67)	76.74–87.62
	Yes	28 (13.86)	9.41–19.41
Airway obstruction	No	170 (84.16)	78.38–88.90
	Yes	32 (15.84)	11.10–21.62
Laryngeal membrane	No	184 (91.09)	86.28–94.63
	Yes	18 (8.91)	5.37–13.72
Respiratory failure	No	172 (85.15)	79.48–89.75
	Yes	30 (14.85)	10.25–20.52
Mortality	No	170 (84.16)	78.38–88.90
	Yes	32 (15.84)	11.10–21.62

the most commonly used antibiotic, the choice of antibiotic did not significantly impact outcomes after adjustment. Most deaths occurred in unvaccinated children, highlighting the ongoing risk posed by inadequate immunization.

The wide confidence interval around the adjusted OR for carditis (95% CI 4.72–88.92) reflects the relatively limited number of deaths ($n = 32$) in this cohort, which constrains the precision of individual odds ratio estimates. This finding should therefore be interpreted with caution. Nonetheless, the magnitude and direction of the association are consistent with the published literature, where diphtheritic myocarditis is well established as the principal determinant of mortality, with CFRs among affected individuals ranging from 20% to 70%.

These features occur due to the underlying pathogenesis of diphtheria. As diphtheria progresses, the toxin-producing *Corynebacterium diphtheriae* induces the development of a thick, tightly adherent grey pseudomembrane over the pharynx, tonsils or larynx. This membrane may bleed upon attempted removal and can cause significant airway obstruction and respiratory distress, sometimes necessitating emergency interventions such as intubation or tracheotomy in severe cases [13]. Systemic absorption of the diphtheria toxin can lead to myocarditis, typically emerging 7 to 14 days after symptom onset. This complication occurs in approximately 10%–25% of cases and is frequently associated with conduction abnormalities, arrhythmias and heart failure [14]. Myocarditis represents a major contributor to diphtheria-related morbidity and mortality, with CFRs in affected individuals ranging from 20% to 70% [15].

Notably, no neurological complications were recorded in this cohort. This is likely attributable to the absence of post-discharge follow-up rather than a true absence of such sequelae, as peripheral neuropathy from diphtheria toxin typically manifests weeks after the acute illness and would not have been captured within our inpatient dataset.

In the current study, the mean age was 8.44 ± 2.69 s. It is increasingly more common in older children and adults. This is most likely due to a lack of necessary booster dosages at 18 months and 5 years of age. A child who has missed a booster dosage is

TABLE 2 | Mortality by demographic and clinical outcomes.

Variable	No *N* = 170 (95% CI)	Yes *N* = 32 (95% CI)	*p*
age	8.42 [2.77] (8.0, 8.8)	8.53 [2.29] (7.7, 9.4)	0.7
gender			0.005
female	88 (51.76) (44%, 59%)	8 (25.00) (12%, 44%)	
male	82 (48.24) (41%, 56%)	24 (75.00) (56%, 88%)	
Antibiotics			0.005
Benzyl penicillin	52 (30.59) (24%, 38%)	2 (6.25) (1.1%, 22%)	
Ceftriaxone	8 (4.71) (2.2%, 9.4%)	0 (0.00) (0.00%, 13%)	
Ceftriaxone in combination with other	12 (7.06) (3.9%, 12%)	2 (6.25) (1.1%, 22%)	
Linezolid	16 (9.41) (5.6%, 15%)	8 (25.00) (12%, 44%)	
Linezolid in combination with other	78 (45.88) (38%, 54%)	18 (56.25) (38%, 73%)	
Meropenem + Ceftriaxone	4 (2.35) (0.76%, 6.3%)	2 (6.25) (1.1%, 22%)	
Vaccination			0.12
Un-vaccinated	105 (61.76) (54%, 69%)	26 (81.25) (63%, 92%)	
Partially vaccinated	38 (22.35) (16%, 30%)	4 (12.50) (4.1%, 30%)	
Vaccinated	27 (15.88) (11%, 22%)	2 (6.25) (1.1%, 22%)	
Stay (days)	5.01 [4.96] (4.3, 5.8)	3.63 [2.98] (2.6, 4.7)	0.016
Duration of illness before admission days	5.44 [1.75] (5.2, 5.7)	4.88 [1.56] (4.3, 5.4)	0.14
Fever	162 (95.29) (91%, 98%)	32 (100.00) (87%, 100%)	0.4
Cough	158 (92.94) (88%, 96%)	30 (93.75) (78%, 99%)	>0.9
Throat pain	140 (82.35) (76%, 88%)	32 (100.00) (87%, 100%)	0.006
Difficulty breathing	44 (25.88) (20%, 33%)	24 (75.00) (56%, 88%)	<0.001
Carditis	10 (6.10) (3.1%, 11%)	18 (58.06) (39%, 75%)	<0.001
Airway obstruction	12 (7.06) (3.9%, 12%)	20 (62.50) (44%, 78%)	<0.001
Respiratory failure	10 (5.88) (3.0%, 11%)	20 (62.50) (44%, 78%)	<0.001
Laryngeal membrane	10 (5.88) (3.0%, 11%)	8 (25.00) (12%, 44%)	0.002

Note: Median (IQR); *n* (%); Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test. Percentages are row-based, representing the proportion within each exposure category. Numbers in parentheses represent column percentages where applicable.

more susceptible to infection due to a drop in antibody titers [16]. Recent Indian studies have reported a shift in diphtheria cases toward older children [17, 18].

Our study demonstrates that the majority of children with diphtheria presented with classic upper respiratory tract symptoms such as fever, cough and odynophagia. A significant proportion progressed to serious complications, notably upper airway obstruction, respiratory failure and myocarditis. These findings are consistent with the study by Dash et al. [19], who reported fever in 97% of cases, sore throat in 67% and airway compromise and myocarditis in 61.7% and 35.4% of patients, respectively. Nawing et al. [20] also reported similar symptomatology in Indonesian children, although the incidence of cardiac complications was comparatively lower at 14.3%. Our observation of diphtheritic cardiotoxicity aligns with the prospective study by Kneen et al. [21], where the presence of extensive pseudomembranes and bull neck was predictive of diphtheritic cardiomyopathy, supported by ECG abnormalities and elevated cardiac enzymes. Similarly, Mohan et al. [12] identified respiratory failure and myocarditis as the leading complications, even in partially or fully immunised children, underscoring the role of waning immunity or incomplete booster coverage.

In this study, linezolid was the most commonly used antibiotic in children with diphtheria. However, after adjustment, the choice of antibiotic was not significantly associated with outcomes, including major complications (e.g., airway obstruction, carditis, respiratory failure) or mortality. This supports existing evidence that clinical outcomes in diphtheria depend more on timely antitoxin administration, airway management and early supportive care, rather than the specific antibiotic

TABLE 3 | Multivariate analysis for mortality by demographic and clinical outcomes.

Variable	Category	No. (%) survived	No. (%) died	Univariable OR (95% CI), *p*	Multivariable OR (95% CI), *p*[a]
Gender	Female	88 (91.7)	8 (8.3)	Reference	Reference
	Male	82 (77.4)	24 (22.6)	3.22 (1.42 to 8.02), 0.007	1.42 (0.45 to 4.55), 0.548
Antibiotics	Ceftriaxone	20 (90.9)	2 (9.1)	Reference	—
	Linezolid	94 (78.3)	26 (21.7)	2.77 (0.74 to 18.03), 0.189	0.73 (0.13 to 6.17), 0.738
	Penicillin	52 (96.3)	2 (3.7)	0.38 (0.04 to 3.38), 0.355	0.29 (0.03 to 3.22), 0.292
Difficulty Breathing	No	126 (94.0)	8 (6.0)	Reference	Reference
	Yes	44 (64.7)	24 (35.3)	8.59 (3.74 to 21.73), <0.001	0.77 (0.12 to 4.05), 0.773
Carditis	No	154 (92.2)	13 (7.8)	Reference	Reference
	Yes	10 (35.7)	18 (64.3)	21.32 (8.41 to 57.89), <0.001	18.50 (4.72 to 88.92), <0.001
Laryngeal Membrane	No	160 (87.0)	24 (13.0)	Reference	Reference
	Yes	10 (55.6)	8 (44.4)	5.33 (1.87 to 14.90), 0.001	1.15 (0.07 to 13.92), 0.920

[a]Logistic regression.

used. Globally, penicillin and erythromycin are recommended as first-line agents [22]. In Pakistan, due to the growing prevalence of macrolide and penicillin resistance, clinicians often use linezolid guided by culture and sensitivity reports, especially in severe or unresponsive cases [23]. While linezolid has proven efficacy in paediatric Gram-positive infections like MRSA [24], there is no high-quality evidence supporting its superiority in diphtheria specifically. Our findings emphasise that while linezolid may be appropriate in resistant cases, its use does not appear to reduce the risk of serious complications or death when compared to standard therapies.

Our study demonstrates that carditis (specifically, myocarditis) is the only independent predictor of mortality in children with diphtheria, even though several clinical variables—such as male sex, respiratory distress and presence of laryngeal membranes—showed significant associations with mortality in univariable analysis. In the multivariable model, however, only cardiac involvement retained statistical significance, with an adjusted odds ratio of 18.50 (95% CI: 4.72–88.92; $p < 0.001$). These findings are consistent with previous research from India. Jayashree et al. also identified myocarditis as the sole independent predictor of death, with an adjusted OR of approximately 0.061 (95% CI: 0.009–0.397; $p = 0.003$), and reported that 85% of fatal outcomes were attributable to cardiac complications [25]. Similar conclusions also emerged from a tertiary-care cohort in Kolkata, where diphtheritic cardiomyopathy was strongly associated with fatal outcomes [19].

Most deaths in our study occurred in unvaccinated children, showing the continued danger of low immunisation rates. This pattern is similar to findings from other studies in the region, which have reported higher death rates in children who were not fully vaccinated against diphtheria, and much lower mortality when vaccination coverage is high [26]. Although male sex, laryngeal membranes and respiratory distress were each linked to a higher risk of death in univariable analysis, they did not remain significant after adjusting for other factors. This is likely because their effect is either explained by or less important than the presence of carditis, which was the strongest factor linked to mortality.

Although vaccination status did not reach statistical significance as an independent predictor of mortality in multivariable analysis ($p = 0.12$), 81.3% of deaths occurred among unvaccinated children, a finding that warrants careful interpretation. Several factors may explain this apparent discrepancy. First, unvaccinated children constituted the majority of the overall cohort (64.9%), meaning the higher absolute number of deaths in this group partly reflects their over-representation in the sample rather than an independent mortality effect. Second, the study was likely underpowered to detect a statistically significant difference in mortality by vaccination status given the total number of events. Third, vaccination status was determined by parental recall or immunization card availability, introducing potential misclassification that would bias the association toward the null. Fourth, unvaccinated children may have experienced a more fulminant disease course, dying early before complications such as carditis could fully manifest and dominate the regression model, which may have further attenuated the independent effect of vaccination status. Despite non-significance in the adjusted analysis, the epidemiological signal remains clear and reinforces the urgent need to improve DPT coverage.

5 | Strengths and Limitations

This study has a relatively large sample of 202 children from a resource-limited, high-burden setting, all diagnosed using WHO-standardised criteria. Data were collected comprehensively across demographics, vaccination history, clinical features, antibiotic use and outcomes, and multivariable logistic regression was used to identify independent predictors of mortality. The fact that all patients received antidiphtheria toxin as

part of their initial treatment also reduces an important source of variability in outcome comparisons.

There are, however, several limitations to consider. The retrospective design carries the risk of documentation bias and incomplete records. Being a single tertiary referral centre, the findings may not represent the full picture of diphtheria at the community level, and the case mix likely skews toward more severe presentations. Vaccination status was based on caregiver recall or immunization cards, which may not always be reliable. The timing and dosing of antidiphtheria toxin were not systematically analysed, and microbiological confirmation was not available for all cases, as diagnosis was based primarily on clinical criteria. Additionally, the anatomical site of pseudomembrane involvement (pharyngeal, laryngeal or nasal) was not consistently documented in the medical records and could not be reliably extracted retrospectively. Long-term outcomes after discharge, including neurological complications and cardiac recovery, were not followed up. The study also only included children aged 5–16 years, which means the findings cannot be extended to infants and younger children.

6 | Conclusion

This study found that mortality is relatively high in children hospitalised with diphtheria, with carditis identified as the most important independent predictor. Although clinical signs such as breathing difficulty, airway obstruction and laryngeal membrane formation were more frequent among non-survivors, only cardiac involvement remained significant after adjustment. The elevated mortality rate, especially among unvaccinated children, highlights the need for early recognition of cardiac complications and the urgent reinforcement of preventive measures, including vaccination programs and timely clinical management, to reduce diphtheria-related deaths.

Author Contributions

Waqas Naseem: conceptualization, investigation, funding acquisition, methodology, validation, visualization, software, formal analysis, project administration, data curation, supervision, resources. **Ashfaq Ahmed:** conceptualization, investigation, funding acquisition, writing – original draft, methodology, validation, visualization, writing – review and editing, software, formal analysis, project administration, supervision, resources, data curation.

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Disclosure

The authors have nothing to report.

Ethics Statement

Ethical Approval was taken by the Institutional Review Board of the Lady Reading Hospital, Peshawar, Pakistan Reference No: 399/LRH/MTI, and our conducted research was in compliance with the Helsinki Declaration.

Consent

Informed consent was obtained from all patients' guardians prior to the use of their anonymised records for research purposes.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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