

Resurgence of Diphtheria; Vaccination Status, Clinical Profile and Outcome of Children Suffering With Diphtheria

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ABSTRACT

Objective: To determine the vaccination status of children suffering from diphtheria, their clinical profile and outcome.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pediatrics, MTI/ Lady Reading Hospital Peshawar from July 2023 to December 2023.

Methods: Data was collected after approval from Hospital ethical committee. Sample size was calculated through Open EPI and non-probability consecutive sampling technique was used. From arrival to departure, patients were followed.

Results: A total of 67 children were included. Of them 40(59.7%) were male and 27(40.3%) were females. Mean age was 8.80 ± 3.43 with range from 2 to 15 years. Out of them 39(58.2%) were unvaccinated, 20(29.9%) were partially vaccinated and 8(11.9%) were routinely vaccinated. 34(50.7%) had mild symptoms at arrival, 23 with bull neck and 10 with serious illness. In 45(67.1%) patients cardiac involvement was present ranging from sinus tachycardia to VT. 08(11.9%) had renal and 05(7.5%) had neurological involvement. 54(80.6%) received ADS and 13(20.4%) couldn't. 12(17.9%) patients unfortunate outcome (died) and 55(82.1%) successfully recovered.

Conclusion: This study shows that Diphtheria has resurged again and the most effective measures, vaccination, is very poor as majority (88%) of our patients are unvaccinated or partially vaccinated. Cardiac involvement is the major complication of diphtheria. A significant number of mortality occurs due to diphtheria and there is insufficiency of ADS for these patients.

Key Words: Diphtheria, vaccination, cardiac complications, Anti-diphtheria serum

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INTRODUCTION

Diphtheria is an infectious disease caused by toxigenic strains of *Corynebacterium diphtheriae*. It is an acute potentially fatal infectious disease.¹ It remained a leading cause of childhood death in the pre-vaccine era.² In industrialized world its incidence fell after WW2 and in developing countries vaccination brought this change following WHO launching of Expanded Programme on Immunization in 1974³.

Diphtheria commonly presents as infection of the upper airways. Skin infection can occur and is usually uncommon.

Most of the time, it presents with complications. Among these are the acute respiratory obstruction, toxic myocarditis and neurologic weakness are the most important complications of diphtheria. Thrombocytopenia, renal failure and septicemia can occur.^{4,5} The clinical presentation and severity of diphtheria vary in immunized and non immunized children. Early diagnosis and prompt treatment including administration of diphtheria antitoxin and antibiotics minimize mortality.⁶

Diphtheria is a vaccine preventable disease. Its vaccination schedule consists of three doses of primary series starting at 06 weeks of age, followed by at 10 and 14 weeks.⁷ This vaccination was devised by WHO in 1974 and implemented all over the world. However due to different reasons, prominently war hit zones, continued to have cases of diphtheria and so this disease couldn't be eradicated. For further reduction in this disease, WHO revised immunization schedule with addition of three booster doses given at 12–23 months of age, 4–7 years, and 9–15 years of age.⁸ Further diphtheria vaccine is safer and has very less adverse effects. Hitt J Sharma et al studied locally prepared

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vaccine for safety and immunogenicity and found it safe and effective.⁹

Since 1980, the number of diphtheria cases gradually declined till early 90s and then had a spike. The disease continued to be reported in less number of cases due to small epidemics occurring from place to place. Factors responsible for these epidemics are reduced immunization, mass migration of population internal and external, conflict zones, poor health facilities and low literacy rates in under-developed countries. World Health Organization shows that diphtheria progressively decline with the advent of vaccination, improved hygiene, properly treatment of diagnosed cases.^{10,11,12} However for last one decade its fall has stopped and is raised as in African region in 2014, 01 was reported but in 2022, 910 cases were reported. Similarly in European Regionn 2014, 35 cases were reported but in 2022, 362 cases were reported. Pakistan diphtheria statistics reported fall to single digit, 09 cases were reported in year 2014 and 2015, last year 2022 raised to 351 and in the current year, 2023, a massive surge is predicted.^{13,14}

Diphtheria was seen occasionally, though not eradicated but in year 2022, 351 cases were reported and in the early time of year 2023, cases seen^{13,14}, were going very high. In july, the pediatric isolation section of our hospital was 70% occupied by diphtheria. So the study was planned to determine the vaccination status, their clinical profile and outcomes in children suffering from diphtheria in the post covid era of 21st century in a tertiary care centre of developing country. Sharing this work will enhance health care professional knowledge about need of vaccination and help in counseling the parents regarding vaccination. Reporting to health authority will sensitize for planning booster vaccination days for children.

Operational Definitions;

Clinical Diphtheria case:

A child will be considered to have clinical diphtheria, if he/she has all of the following;

1. Temperature more than 38 c
2. Have upper respiratory tract infection (pharyngitis, tonsillitis, or laryngitis)
3. Grayish membrane on tonsils, pharynx, nose or larynx assessed by one pediatric consultant and one ENT Consultant

Confirmed Diphtheria case:

A child will be considered to have confirmed diphtheria, if he/she has all of the following;

1. Temperature more than 38 c
2. Have upper respiratory tract infection (pharyngitis, tonsillitis, or laryngitis)
3. Grayish membrane on tonsils, pharynx, nose or larynx
4. Throat or Nose swab culture shows *Corynebacterium diphtheriae*

METHODS

Setting; Department of Pediatrics, MTI/Lady Reading Hospital Peshawar

Study Design; Descriptive cross-sectional study

Study Duration: 4 months after study proposal approval

Sample size:

A total of 39 cases will be studied as calculated from WHO statistics with incidence of 2.6 %, keeping confidence interval of 95% and margin of error of 5%.

Inclusion Criteria;

All newly diagnosed cases of diphtheria under the age of 15 years as per operational definition.

Both Genders

Exclusion Criteria;

Children with upper respiratory tract infection with alternative diagnosis will be excluded like;

1. Acute follicular tonsillitis.
2. Viral croup
3. Epiglottitis
4. Retropharyngeal abscess.
5. Previously diagnosed cases of diphtheria and now with complications or other disease

Data Collection and Analysis:

After approval from hospital ethical committee, data was collected after taking informed consent from parents of patient. Data was recorded in specially prepared proforma for this purpose. Demographic data, vaccination status, clinical features, complication and outcome was recorded. After completion of the data collection, data was analyzed using SPSS, version 24. Quantitative variables like age was calculated as mean and + SD. Frequency and percentages were calculated for categorical variables like gender, vaccination status, clinical profile, treatment received, complications and outcome. Results are presented in tables and charts.

RESULTS

A total of 67 children were included. Of them 40(59.7%) were male and 27(40.3%) were females. Mean age was 8.80±3.43 with range from 2 to 15 years. Out of them 39(58.2%) were unvaccinated, 20(29.9%) were partially vaccinated and 8(11.9%) were routinely vaccinated (Fig 1).

Clinical profile shows 34(50.7%) had mild symptoms at arrival, 23 with bull neck and 10 with serious illness.(Fig 2)

Regarding complications, in 45(67.1%) patients cardiac involvement was present ranging from sinus tachycardia to VT. 08(11.9%) had renal and 05(7.5%) had neurological involvement. 54(80.6%) received ADS and 13(19.4%) couldn't. (table 1)

Outcome was unfortunate (died) in 12(17.9%) patients and successful in 55(82.1%) (discharge well). (table 2)

Area wise distribution is shown in chamber 3, showing patients be referred from all areas of the province. (fig 3)

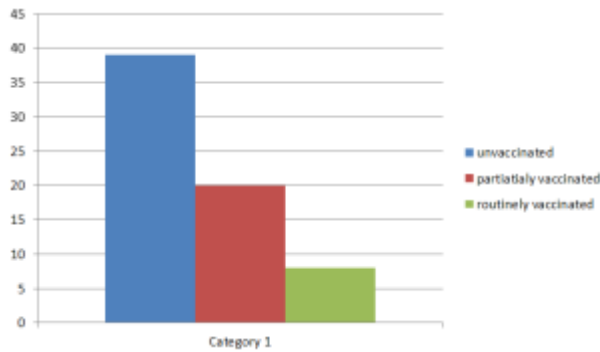


Figure No.1: Vaccination status of children suffering from diphtheria

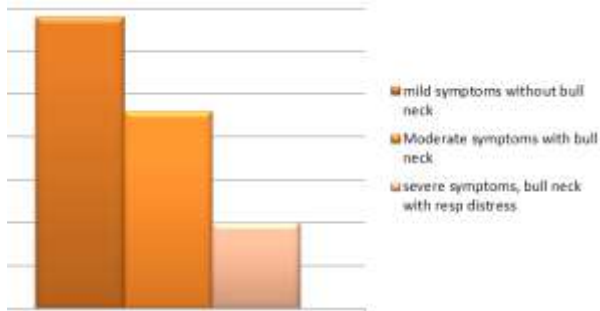


Figure No.2: Clinical presentation of children with diphtheria at arrival

Table No.1: Complications of diphtheria in children and ADS receiving status

Feature	Cardiac involvement	Renal Involvement	Neurological involvement	ADS not received
Frequency	45	08	05	13
Percentage	67.1%	11.9%	7.5%	19.4%

Table No.2: Outcome of children with diphtheria

Serial No	Outcome	Number of patients	Percentage (%)
1	Recovered	55	80.6
2	Expired	12	19.4
3	Total	67	100

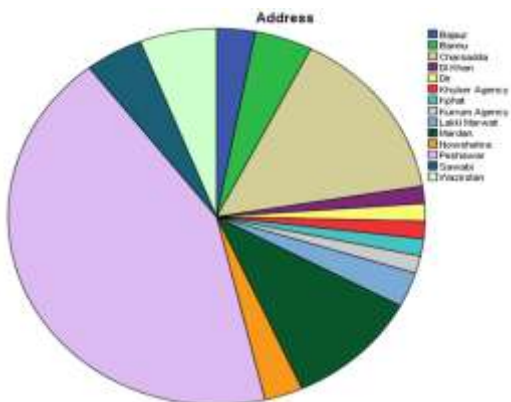


Figure No.3: Area wise distribution of diphtheria patients



Figure No. 4: Picture of a child with tonsillar diphtheria



Figure No.5: Rhythm disorder in a child with diphtheria

DISCUSSION

Diphtheria, vaccine preventable disease, is reemerging again as is evident by the reports of several authors and World Health Organization’s statistics of infectious diseases¹³. Multiple factors are involved in its resurgence but insufficient vaccination and massive migration due to war are the most significant factors. Inadequate vaccination results in not achieving herd immunity and spread of the disease among the community. Similarly war not only affects vaccination status of children in the conflict zone but also spread disease to healthy community through massive migration.¹⁵

Pakistan is a war hit zone for last 04 decades and remained largest refugees’ recipient from Afghanistan since USSR-Afghan war. Even then Pakistan struggled to achieve maximum improvement in health and improve vaccination.¹⁶ To a large part it remain successful and infectious diseases fell significantly as can be seen in WHO statistics available online which shows that diphtheria fall to single digit in 2014 in Pakistan.¹³ But the covid-19, financial constraints and the impact of long war inside and in neighborhood, lead to Pakistan of not getting the goals.^{13,14}

We have noted last year a rise in diphtheria cases to 351 were reported,¹³ and this year (2023), it was much higher. In our study a total of 67 children with diphtheria were included. Of them 40(59.7%) were male and 27(40.3%) were females. Mean age was 8.80 ± 3.43 with range from 2 to 15 years. Out of them

39(58.2%) were unvaccinated, 20(29.9%) were partially vaccinated and 8(11.9%) were routinely vaccinated. 34(50.7%) had mild symptoms at arrival, 23 with bull neck and 10 with serious illness. In 45(67.1%) patients cardiac involvement was present ranging from sinus tachycardia to VT. 08(11.9%) had renal and 05(7.5%) had neurological involvement. 54(80.6%) received ADS and 13(19.4%) couldn't. 12(17.9%) patients unfortunate outcome (died) and 55(82.1%) successfully recovered.

Ray SK et al¹⁷ noted a very poor vaccination status in his study. He found that only 27.4% of patients with diphtheria were fully vaccinated while 44.4% were partially vaccinated and 28.2% were unvaccinated.¹⁸ Our findings were more dreadful as only 8(11.9%) were vaccinated as per WHO EPI schedule while 34(50.7%) were not vaccinated and 20 (29.9%) partially vaccinated. However, Sharma S et al¹⁸ in his study found 59% completely vaccinated, 10% partially vaccinated and 31% unvaccinated, a comparatively better vaccination status compared to our finding. He further found that complications were more common in unvaccinated patients than vaccinated which was statistically significant with P value of < 0.05. However, neurological complications were equal in all patients, irrespective of vaccination status.¹⁸

The clinical presentation was divided in to three groups; with mild symptoms, with bull neck without airway compromised and with serious disease. Mild symptoms were present at presentation were present in 34(50.7%), 23(34.3%) had bull neck without airway compromised, while 10(14.9%) were received in serious illness. Anjum S et al¹⁹ in their study found that 88.7% had throat pain and cervical lymphadenopathy and 14.7% with typical bull neck, a comparable to our study. Similar clinical presentation findings were reported by Kamath L et al in Karnataka, India²⁰.

The common complications noted in our study were cardiac involvement in 45(67.1%) patients, renal in 08(11.9%) and neurological 05(7.5%). Cardiac complications varied in its pattern and were difficult in management. Jamar SK et al reported neurological complications in children with diphtheria as the most common 20.3%, followed by cardiac 17.5% and bronchopneumonia 8.2%.²¹ This contrasts to our study where cardiac complications are the commonest. However Ray SK et al reported 53.9% of patient with diphtheria had complications and the commonest was myocarditis, 29.8%, followed by neurological 12% and respiratory 7.1%.¹⁸ They didn't mention renal complications, found in 11.9% of our patients.^{17,18,21}

The outcome was not successful in 17.9% of our patients. All patients who had this unsuccessful outcome had cardiac involvement. SN Singh et al reported mortality of 48%, quite higher than our findings; however this could be due to severe disease at presentation and airway complications as mentioned in

work.²² Boughani S et al reported mortality of 5.4% in his study a quite good than other centers; however his study was based secondary data from government of the same and any short comings may have impact on the results.²³ It is worth mentioning that 19.4% of our patients couldn't receive ADS (Anti Diphtheria Serum), one of the important treatment and preventive modality after vaccination.

CONCLUSION

- This study shows that Diphtheria has resurged as 67 patients documented in this study from one center is highly alarming.
- Cases reported from all over province signifies the spread of the diphtheria.
- The most effective measure, vaccination, is very poor as majority (88%) of our patients is unvaccinated or partially vaccinated.
- Half of the patients presented with moderate to severe disease.
- Cardiac involvement is the major complication of diphtheria.
- Diphtheria has high mortality despite treating in a tertiary care center. So the primary prevention is the best strategy in combating diphtheria.

Author's Contribution:

Concept & Design of Study:	Afzal Khan
Drafting:	Lal Muhammad, Rabiya Munir
Data Analysis:	Sajid Ali, Zainab Rahman, Alia Abdulhaq
Revisiting Critically:	Afzal Khan, Lal Muhammad
Final Approval of version:	Afzal Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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