International Journal of Contemporary Pediatrics
Bhatnagar R et al. Int J Contemp Pediatr. 2020 Jan;7(1):149-153
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20195744

Original Research Article

Resurgence of diphtheria and its outcome among children in western Uttar Pradesh: a battle to conquer

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Received: 18 October 2019
Revised: 08 November 2019
Accepted: 14 November 2019

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ABSTRACT

Background: Considered as a rare clinical entity in immediate post-vaccination era, diphtheria has now started gaining surface in India for last few years, with an epidemiological shift involving older children owing to poor immunization coverage and waning immunity. Thus, it is imperative to quantify disease burden, analyses the clinical profile and factors affecting the outcome of diphtheria in children.
Methods: A prospective observational study conducted in the Pediatric department of a teaching hospital where all children admitted with clinical diagnosis of diphtheria during the study period were included. Demographic data and clinically relevant information along with complications and outcome were recorded. Cases were managed as per standard treatment protocol providing intensive care support wherever required. Complications and factors affecting the outcome in all diphtheria cases were analysed.
Results: Total 53 children were enrolled into study, and the mean age of study population was 7.55±2 years. Fever, pseudo membrane and throat pain were observed in all the cases. Palatal palsy was the earliest and the commonest complication (60.4%) followed by myocarditis (55%). Case fatality rate was 33.9% and myocarditis (77%) was the commonest complication attributing to it. Poor immunization status, late presentation and delayed ADS administration were associated with increased complication rate and unfavorable outcome.
Conclusions: Robust immunization activity coupled with improved case-based surveillance would go a long way in preventing further diphtheria outbreaks in community. Sensitization about this re-emerging disease and high index of suspicion in diagnosing it, amongst primary care physicians and peripheral health workers would promote early referral and prompt management thereby reducing morbidity and high mortality associated with diphtheria.

Keywords: Diphtheria, Immunization, Myocarditis, Palatal palsy, Pseudo membrane

INTRODUCTION

Diphtheria is a tropical infectious disease, potentially fatal and caused by toxigenic strains of Corynebacterium diphtheriae. It localizes in the upper respiratory tract and the resulting ulceration and inflammation induces the formation of pseudo membrane, a pathognomic feature of the disease. The potent exotoxin derived from the microorganism gets absorbed into the circulation and damages remote organs, mainly myocardium and peripheral nerves. The mortality rate, which is generally 5-10%, may be as high as 20% in children below 5 years of age.[1]

Vaccination against diphtheria has reduced the mortality and morbidity of diphtheria dramatically, however it is still a significant child health problem in countries with poor immunization coverage.[2] In 2017, a total of 8,819 cases of diphtheria were reported worldwide, India has

reported the largest proportion of diphtheria cases (64%) in aggregate data since year 2000.[3]

In the last few years, the country has witnessed unusual surge in diphtheria cases after showing a remarkable reduction in the year 2015.[4] Re-emergence of this dreadful disease reflects inadequate immunization coverage, waning immunity and lack of awareness about booster vaccination. As per the Vaccine Preventable Surveillance (VPD) data, 1307 diphtheria cases have been reported from Uttar Pradesh.[5] Literature has described sufficient information on diphtheritic illness in children but detailed studies on its outcome and factors affecting its morbidity and mortality are lacking in Uttar Pradesh.

The present study intends to estimate the frequency of diphtheria in children and analyse the factors associated with its morbidity and mortality. It also aimed at creating awareness among the general physicians, health care workers and caregivers, regarding its resurgence in post vaccination era, which is imperative for timed diagnosis and prompt management of this vaccine preventable disease. Thus, strengthening the immunization coverage is need of the hour as also highlighted by this study.

METHODS

A prospective observational study was conducted in the Pediatric ward of a teaching hospital from May 2016 for 30 months. After seeking approval from the Institutional Ethics Committee and taking written informed consent from the parents, all children admitted with clinical diagnosis of diphtheria were enrolled into the study. WHO guidelines were used to define cases as suspected, probable and confirmed.[6] Cases of membranous tonsillitis secondary to other microorganisms as revealed through culture and gram staining reports, and children presenting with late onset palatal palsy, respiratory paralysis and lower limb weakness in absence of fever, throat pain and pseudo membrane, constituted the exclusion criteria for this study. Detailed history and clinical examination were done in all the cases. Immunization history was documented as per the information given by parents. All those children vaccinated with 3 primary doses of DPT/Pentavalent vaccine at 4 weeks interval followed by booster doses at 16-24 months and at 5 years of age were labelled as immunized, while those who had missed any of the primary or booster doses were said to be partially immunized. Unimmunized children were the ones who had not received any dose of DPT/Pentavalent vaccine. Throat swab for Albert staining and culture were sent . All cases were subjected to immediate treatment with antibiotics, anri-diphtheritic serum(ADS) as per the standard protocol.[7] Complications like myocarditis, respiratory failure, airway obstruction etc were managed in the Pediatric Intensive Care Unit(PICU) of the hospital.

Fifty three children who fulfilled inclusion criteria were enrolled into the study. Clinical outcome was defined as survival or death. Complications and outcome were analysed with respect to demographic and clinical profile in all the cases. Statistical tests applied for qualitative and quantitative data were chi square test and student t-test respectively using SPSS Software version 17, p value of <0.05 was considered to be statistically significant.

RESULTS

During the study period of 30 months, 57 children were admitted with the clinical diagnosis of diphtheria, of which 4 left against medical advice. Thus total 53 children were enrolled into the study for final analysis. The clinical profile of study population is shown in (Table 1).The mean age of study population was 7.55±2.01 yrs. Male to female ratio was found to be 1.8:1 Majority of children with diphtheria were in the age group ranging between 5-10 yrs. Fever and pseudo membrane was the consistent finding in all the cases. The earliest and the commonest complication was palatal palsy observed in 60.4% of the cases followed by myocarditis (55%). Antidiphtheritic serum was administered in 42 cases, as financial constraints precluded its use in the remaining ones (Table 1).

Table 1: Clinical profile of 53 children with diphtheria.

Parameters	N=53	%
Site of pseudo membrane		
Pharyngeal	29	54.7%
Faucial	13	24.5%
Laryngeal	11	20.7%
Immunization status		
Unimmunized	36	67.9%
Partially immunized	12	22.6%
immunized	5	9.4%
Albert stain positive	6	11.3%
Clinical features		
Fever	53	100%
Pseudo membrane	53	100%
Throat pain	53	100%
Difficulty in swallowing	48	90.5%
Neck swelling	32	60.3%
Hoarseness of voice	13	75.4%
Stridor	11	24.5%
Complications		
Early palatal palsy	32	60.4%
Myocarditis	29	54.7%
Airway obstruction	6	11.3%
Respiratory muscle weakness	5	9.4%
Acute renal failure	5	9.4%

Of 29 patients with myocarditis, 21 developed tachyarrhythmia while 4 patients presented each with atrioventricular block and cardiogenic shock respectively. Higher mortality (78%) was associated with myocarditis and found to have statistically significant association with overall mortality in diphtheria cases in this study. Lack of

protective immunity as depicted by immunization status and prolonged duration of symptoms before seeking hospitalization were found to have statistically significant association with development of myocarditis in these children. (Table 2).

Table 2: Correlation of myocarditis with various factors in diphtheria cases

Variables	Myocarditis(n=29) %	No myocarditis(n=24) %	p value
Age(years)	8.5±2	6±2	0.66
Unimmunized	23(79%)	13(54%)	0.00
Partially immunized	5(17%)	7(29%)	0.00
Immunized	1(3%)	4(16%)	0.00
Pharyngeal diphtheria	19(65%)	10(41%)	0.8
Laryngeal diphtheria	5(17%)	6(25%)	0.8
Faucial diphtheria	5(17%)	8(33%)	0.8
Duration of symptoms(days)	5.4±1.5	5±1.5	0.016
Mortality	14(78%)	4(22%)	0.013

Out of 53 patients, 18 patients died with case fatality rate of 33.9%. The most common cause of mortality was myocarditis (78%) followed by acute renal failure (14%) and respiratory muscle paralysis (8%). The immunization status and duration of symptoms had statistically significant association with outcome of diphtheria cases, as there was no mortality in immunized group. In contrast to it, 15 and 3 deaths were in the unimmunized and partially immunized group respectively. Early ADS administration proved to have statistically significant association with favourable outcome in these children (Table 3).

Table 3: Correlation of outcome with various factors in diphtheria cases.

Variables	Non-survivors n=18(%)	Survivors n=24(%)	p value
Age (yrs)	7±3.3	8.6±2.6	0.47
Unimmunized	15(42%)	21(58%)	0.00
Partially immunized	3(25%)	9(75%)	0.00
Immunized	0	5(100%)	0.00
Duration of symptoms(days)	4.8±2.3	4.2±1.6	0.23
Time of ADS administration(days)	5.89±2.8	5.0±1.9	0.03

DISCUSSION

Diphtheria, an acute infectious disease of potential morbidity and mortality became a forgotten entity in the past owing to effective vaccine and robust immunization coverage against it. Current statistics show that diphtheria has been re-emerging in India.[4] This phenomenon is attributable to inadequate vaccine coverage and declining immunity in adolescents and adults. Considering this fact, in 2016 National Technical Advisory Group on Immunization (NTAGI), decided to replace TT (Tetanus toxoid) vaccine with Td (Tetanus diphtheria-adult) vaccine at 10 and 16 years of age to protect adolescent-adult population from diphtheria. It has been incorporated into Universal Immunization Programme (UIP) by the end of year 2018 in a phased manner.

In this study, resurgence of diphtheria was commonly observed in older children belonging to age group of 5-10 yrs, suggesting epidemiological shift in the disease. Similar observation was reported by various authors.[8,9]

According to National Family Health Survey-4 (2015-16), the immunization coverage in India is 62% and the coverage of three primary doses of diphtheria vaccine is 78.4%.[10] It does not estimate the coverage of diphtheria booster which is expected to be low. With the advent of Intensified Mission Indra Dhanush launched in 2017, an average of 18.5% increase in immunization coverage has been reported.[11] This study showed dismal state of immunization in the region with 67.9% unimmunized cases while partially immunized cases correspond to 22.6%. Occurrence of diphtheria amongst immunized cases (9.4%) as reported through this study, suggest reduced efficacy of vaccine due to breach in cold chain or inappropriate dose/ site of administration etc. Murhekar in 2017 compared various published studies on diphtheria within different states and concluded that diphtheria among school going children and adolescents reflect waning immunity or missed booster dose, while cases under five years of age indicate inadequate coverage of primary diphtheria vaccine.[12]

The upper respiratory tract mucosa is the most common site of infection in this illness, which gets inflamed and ulcerated to form pseudo membrane. Fever, pseudo membrane (pathognomic feature) and throat pain were the consistent finding in all cases of diphtheria in this study. Depending upon the location of pseudo membrane, cases were defined as pharyngeal, faucial and laryngeal

which correspond to 54.7%, 24.5% and 20.7% of the total cases respectively. On the contrary, Jayashree et al, found faucial (73%) involvement as the commonest site followed by pharyngo laryngeal (25%) and laryngeal (1%) amongst 48 children with diphtheria in their study.[13]

Owing to prior antibiotic usage, incorrect method of sample collection and delayed inoculation onto the selective media, microbiological confirmation was obtained only in 6 cases. Similar observation of lower bacteriological yield was reported by Patel et al, and Ray et al, in their studies on diphtheria.[14,15] This calls attention to make prompt clinical diagnosis in such cases while ruling out other masquerading conditions presenting with fever and membrane in throat, so that judicious use of ADS and antibiotics could be instituted at the earliest.

Diphtheria infection may prove lethal due to its toxin mediated damage on myocardium leading to arrhythmias, conduction blocks and cardiogenic shock. Toxic cardiomyopathy occurs in 10-25% of patients with respiratory diphtheria and is responsible for 50-60% of deaths.[7]Author found myocarditis as the second most common (54.7%) and the most fatal complication of diphtheria. Of 29 cases with myocarditis, 14(77.7%) succumbed due to underlying ventricular tachycardia and cardiogenic shock. Jayashree et al, reported 32 patients with myocarditis of which 25(78.1%) died, similar results were obtained by Meshram et al.[13,9] In this study, it was observed that inadequate immunity and prolonged illness had significant association with development of myocarditis. Thus, re-emphasizing the role of early diagnosis and prompt management of this dreadful disease, which may further ameliorate the subsequent development of such devastating complication in these patients.

Neurologic complications parallel the severity of primary infection and are multiphasic in onset.[7] The first indication of neuropathy is paralysis of soft palate and posterior pharyngeal wall. Palatal palsy was the earliest and commonest complication (60.4%) reported in this study, manifesting within 2 weeks of the onset of illness and associated with uneventful recovery in isolated cases. This finding was in accordance with the studies done by Arya et al, who observed palatal palsy(18.5%) as the commonest neurological complication and Manikyamba et al, also reported isolated palatal palsy in 56% cases.[16,17] None of the studies evaluated the outcome of palatal palsy in diphtheria cases. Respiratory failure due to diaphragmatic muscle weakness was seen in 5% of cases. True estimation of diphtheritic polyneuropathy cases could not be done as it was not a follow up study.

The exotoxin of C. diphtheria also affects the renal parenchyma resulting in acute renal failure. Author reported 5 cases of acute renal failure in this series, of which 2 underwent hemodialysis and recovered uneventfully, 3 expired due to concomitant occurrence of myocarditis in them. Similar finding was observed by other authors.[9,13,18]

Of total 53 diphtheria cases, 18 expired resulting in case fatality rate of 33.9%. similar to reports from different centres (32-56.3%) in north India.[9,17] Late presentation when complications had already been set in, delayed ADS administration, financial constraints by care givers attributed to high case fatality rate in this series. This study made an important observation with regards to immunization status and disease related morbidity and fatality, as complete survival was observed in fully immunized group. The mortality was significantly higher (p 0.000) in unimmunized and partially immunized children in this study.

The rebound return of diphtheria in this study clearly demonstrates, how rapidly success can be reversed when efforts like immunization coverage lag. Ministry of Health and Family Welfare, Government of India has launched a mobile application to make parents and guardians aware about the immunization schedule of their children and for tracking their immunization status.[19]

CONCLUSION

With the help of robust immunization activity and effective case-based surveillance system, India has attained polio eradication and measles elimination. Similar targeted approach is the need of the hour for achieving diphtheria control especially in the face of its resurgence in the country. Immunization coverage of 90% is required to attain herd immunity, thereby preventing diphtheria outbreaks in the susceptible community. Thus, coverage of primary and booster diphtheria vaccination needs to be re-emphasized & strengthened through peripheral health workers and primary care physicians.

Being the disease, which primarily affects the underprivileged and ignorant strata of the society, spreading awareness about its re-emergence and its associated fatal complications, may promote early seeking of medical care by them. Prompt diagnosis and timed administration of antibiotics along with ADS plays a pivotal role in reducing the transmission of diphtheria and its related comorbidities. This calls for keeping high index of suspicion by health care personnel while evaluating cases of membranous tonsillitis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, editors. Diphtheria. In: Epidemiology and Prevention of Vaccine-preventable Diseases. 10th ed. Washington, DC: Public Health Foundation; 2007:59-70.

2. World Health Organization. Diphtheria. Available at:https://www.who.int/immunization/diseases/diphtheria/en/. Accessed 30 September 2019.
3. Clarke KE, MacNeil A, Hadler S, Scott C, Tiwari TS, Cherian T. Global Epidemiology of Diphtheria, 2000–2017. Emerg Infect Dis. 2019;25(10):1834.
4. World Health Organization. WHO vaccine-preventable diseases: monitoring system 2019 global summary. Available at: https://apps.who.int/immunization_monitoring/globalsummary/timeseries/tsincidencediphtheria.html. Accessed 28 September 2019.
5. Ministry of Health and Family Welfare, Govt. of India. Integrated Disease Surveillance Programme. Available at: https://www.idsp.nic.in/. Accessed 12 September 2019.
6. Begg N. World Health Organization. Manual for the Management and Control of Diphtheria in the European Region. Copenhagen: WHO Regional Office for Europe; 1994.
7. Buescher ES. Diphtheria. In: Kliegman RM, Stanton BF, St Geme J, Schor NF. Nelson Textbook of Pediatrics. 20th ed. Philadelphia PA: Elsevier; 2016:1347-48
8. Sachin KR, Ramesh H, Sachin KG, Siddharth ES. The outcome of resurgence of diphtheria in older children in a tertiary care hospital. Int J Contemp Pediatr. 2019;6:607-10.
9. Meshram RM, Patil A. Clinical profile and outcome of diphtheria in central India: a retrospective observational study. Int J Contemp Pediatr. 2018;5:1600-5.
10. IIPS O. National Family Health Survey (NFHS-3), 2005-06: India. Vol. I. Mumbai: International Institute for Population Sciences. 2007.
11. National Health Mission. Intensified Mission Indra Dhanush. Available at: https://nhm.gov.in/New_Updates_2018/NHM_Components/Immunization/Guildelines_for_immunization/IMI_CES_Survey_Report.pdf. Accessed 3 October 2019.
12. Murhekar M. Epidemiology of Diphtheria in India, 1996-2016: implications for prevention and control. Am J Trop Med Hygiene. 2017;97(2):313-8.
13. Jayashree M, Shruti N, Singhi S. Predictors of outcome in patients with diphtheria receiving intensive care. Ind Pediatr. 2006;43(17):155-60
14. Patel UV, Patel BH, Bhavsar BS, Dhabi HM, Doshi SK. A retrospective study of diphtheria in Rajkot, Gujarat. Ind J Commu Med. 2004;20:161-3.
15. Ray SK, Das SG, Saha I. A report of diphtheria surveillance from a rural medical college hospital. J Ind Med Assoc. 1998;96(8):236-8.
16. Maharia MS. A clinical study of complications of diphtheria. Intern J Otorhinolaryngol Head Neck Surg. 2019;5(4):1052.
17. Manikyamba D, Satyavani A, Deepa P. Diphtheritic polyneuropathy in the wake of resurgence of diphtheria. J Pediatr Neurosci. 2015;10:331-4.
18. Singh SN, Singh A, Chandra S. Clinical profile and predictors of poor outcome of hospitalized diphtheria cases in children from Lucknow region of North India. Clin Epidemiol Global Health. 2014;2(2):75-9.
19. National Health Portal of India. World Immunisation Week 2019. Available at: https://www.nhp.gov.in/world-immunization-week-2019_pg. Accessed 3 August 2019.

Cite this article as: Bhatnagar R, Sahai L. Resurgence of diphtheria and its outcome among children in western Uttar Pradesh: a battle to conquer. Int J Contemp Pediatr 2020;7:149-53.