

Sporadic Outbreaks of Diphtheria: A Three Year Study from a Tertiary Care Centre of Northeast India.

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Abstract: Diphtheria is an acute toxin mediated contagious febrile illness, predominantly in children, caused by the locally invasive Gram positive bacillus *Corynebacterium diphtheriae*. In developing countries, with increasing coverage of immunization, the incidence of the disease has declined. This study was carried out to know the incidence of diphtheria among 99 patients from suspected sporadic diphtheria outbreaks, admitted in a tertiary care centre of Assam in Northeast India, over a period of three years from January, 2013 to December, 2015. Throat swabs were collected and subjected to direct smear microscopy by Gram's and Albert stains, and culture on Blood agar, Loeffler's serum and Tellurite Blood agar media. *C. diphtheriae* was isolated in 26 cases. The highest culture positivity of 40% each was in age groups 5-9 and 10-14 years. Culture positivity was highest (62.5%) in non-immunized patients, and surprisingly, it was 31.57% in fully immunized patients. The study signifies re-emergence of diphtheria in this State calling for intensive monitoring and review of Universal Immunization Programme, and quality, storage and transport conditions of vaccines in the State.

Keywords: *Corynebacterium diphtheriae*, Kleb-Loeffler's bacillus, immunization, UIP and toxin.

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I. Introduction

Diphtheria is an acute toxin mediated contagious febrile illness, predominantly in children, caused by the locally invasive Gram positive bacillus *Corynebacterium diphtheriae*. It spreads through droplet infection from cases, carriers or close contacts. Diphtheria typically presents as a form of severe pharyngitis with a tough adherent pharyngeal membrane which may extend to the larynx and trachea causing suffocation, and which may bleed on touch.¹ Diphtheria toxin is absorbed into the circulation and can cause myocardial and neurological damages.¹ The severity of the disease is related to the degree of obstruction of the upper respiratory tract caused by an acute bacterial toxin. Overall, the case fatality rate may be as high as 20% to 30% in the toxic form.²

In developing countries with increasing immunization coverage, the incidence of the disease has also been declining.³ However as per data on vaccine-preventable diseases provided by the WHO, India alone accounted for 83.3% of the global burden of Diphtheria in 2014.⁴ According to a report by CDC, USA, India is among the top ten countries with the largest number of reported cases since 2000.⁵ National Health Profiles data of Government of India (CBHI, 2011) showed that the number of reported cases of diphtheria in Assam increased from 894 (no death) in 2011 to 1450 (no death) during 2013 while seventeen deaths reported out of 506 cases during the year 2014.⁶ Various outbreaks of diphtheria were reported earlier from the different parts of Assam with case fatality rate up to 30 per cent.⁷⁻¹⁰

The present study was carried out to know the status of suspected diphtheria cases in children and adults, admitted in our hospital, and the relationship between the clinical disease and the status of immunization of these cases.

II. Material And Methods

The study was conducted over a period of three years from January, 2013 to December, 2015, in the Department of Microbiology, Gauhati Medical College & Hospital (GMCH), Guwahati, Assam. Institutional Ethical Committee clearance was duly obtained. The WHO case definition for surveillance of diphtheria was followed for ascertaining the probable and confirmatory diagnosis of patients.

The subjects of the study included a total of 99 patients with clinical diagnosis of diphtheria, coming from the lower Assam districts, and admitted in GMCH, during the study period. The inclusion criteria of the study cases were, -an illness of the upper respiratory tract characterized by laryngitis or pharyngitis and an

adherent membrane of tonsils, pharynx and/or nose as per the US Centers for Disease Control and Prevention.¹¹

Sample Collection and Processing: Two samples of throat swabs were collected from each case, one for direct microscopy and another for culture, after taking written informed consents. For direct microscopy, smears were prepared and stained with Gram stain and Albert stain to look for Gram positive bacilli and Kleb-Loeffler’s bacilli (KLB). The other throat swab was immediately inoculated on Blood agar, Loeffler’s serum slope and Tellurite Blood agar media, and incubated at 37⁰C for 24 to 48 hours. Typical colonies grown on the media were picked up and stained with Gram stain and Albert stain and examined under microscope to look for Gram positive bacilli and typical diphtheria bacilli.

III. Result

Out of the total of 99 cases, 40 cases were detected/diagnosed in 2013, 28 in 2014 and 31 in 2015. The highest number of 35 cases (35.3%) were in the age group 5-9 years, followed by 25(25.2%) in age group 15-45 years, 20 (20.2%) in 10-14 years, 16(16.1%) in 0-4 years, and the lowest number of 3(3%) cases were aged >45 years. **(Table-1).**

Twenty-six (26.26%) cases of the study were positive for diphtheria both by direct smear microscopy and by culture. Four (4.04%) cases were positive by direct smear microscopy but were negative in culture. **(Table-3).**

Culture positivity rates among cases admitted in 2013, 2014 and 2015 were 15%, 57.14% and 12.9%, respectively (not shown in table). In patients agewise, *C. diphtheriae* was isolated in 14(40%) out of 35 cases in the age group 5-9 years, 8(40%) out of 20 in age group 10-14 years, 3(12%) out of 25 cases in age group 15-45 years, 1(6.25%) out of 16 in age group 0-4 years. None of the 3 cases aged >45 years yielded *C. diphtheriae*. Overall, out of the total of 26 culture positive cases, the highest culture positivity rate of 53.84% was in cases aged 5-9 years, followed by 30.76% in cases aged 10-14 years, 11.53% in cases aged 15-45 years, and 3.84% in 0-4 year’s age group. **(Table-3).**

C. diphtheriae was isolated in 17 (30.35%) of 56 male cases and 9 (20.93%) of 43 female cases. And out of the total 26 culture positive cases, more males (65.38%) than females (34.62%) yielded *C. diphtheriae* in culture. Gender wise distribution showed a male predominance (Male to Female ratio is 56:43). **(Table-2+4).**

As per the history of immunization obtained, out of 99 study patients, 19 were fully immunized, 13 were partially or incompletely immunized, 8 patients were not immunized at all. The status of immunization of the rest 59 patients was not available due to ignorance and illiteracy of those patients and/or their attendants. Culture positivity was highest in non-immunized patients (62.5%), and surprisingly, culture positivity was observed in 31.58% of the fully immunized patients. Among the patients with unknown status of immunization, 23.72% were culture positive, and in partially or incompletely immunized patients, culture positivity was observed in 7.69%.**(Table-5).**

Clinically, all of the 99 cases of the study had mild to moderate fever and sore throat. Pseudomembrane formation in throat was seen in 26 cases that had very mild dyspnoea also. None of the cases had symptoms and signs of myocarditis, polyneuritis, cranial nerve palsies, and secondary pneumonia. The twenty six cases presenting with pseudomembrane formation with mild dyspnoea were found to be positive for diphtheria bacilli both in direct smear microscopy and in culture. Regarding clinical features and immunization status, it was observed that all categories of cases – fully immunized, partially immunized and non immunized, clinical features were the same viz., fever, sore throat, mild dyspnoea and pseudomembrane formation (not shown in separate table or chart).

Table-1: Showing the age wise distribution of the suspected diphtheria cases:

TOTAL	Age Group in years					Year
	>45	15 - 45	10 - 14	5 - 9	0 - 4	
40	3	10	3	13	11	2013
28	0	4	11	12	1	2014
31	0	11	6	10	3	2015
99 (100%)	3 (3.03%)	25 (25.25%)	20 (20.20%)	35 (35.35%)	16 (16.16%)	Total

Table-2: Showing the gender wise distribution of suspected diphtheria cases :

Total	Female	Male	Year
40	18	22	2013
28	15	13	2014

31	10	21	2015
99 (100%)	43 (43.43%)	56 (56.56%)	Total

Table-3: Showing correlation between age of patient and smear/culture positivity:

Smear+ve Culture +ve	Total Cases	Age Group In yrs
1(6.25%) (3.84%)	16	0 - 4
14(40%) (53.84%)	35	5 - 9
8(40%) (30.76%)	20	10 - 14
3(12%) (11.53%)	25	15 - 45
0	3	>45
26(26.26%) (100%)	99	Total

Table-4: Showing correlation between gender of patient and smear/culture positivity:

Smear+ve Culture +ve	Total Cases	Gender
17 (30.35%) (65.38%)	56	Male
9 (20.93%) (34.62%)	43	Female
26(26.26%)	99	TOTAL

Table-5: Showing the correlation between Immunization Status and Culture positivity

Culture +ve	UI* Cases	Culture +ve	NI* Cases	Culture +ve	PI* Case	Culture +ve	FI* Cases	Total Cases	Year
0	6	2	5	0	12	4	17	40	2013
10	22	3	3	1	1	2	2	28	2014
4	31	-	-	-	-	-	-	31	2015
14 (23.72%)	59	5 (62.5%)	8	1 (7.69%)	13	6 (31.58%)	19	99	Total

* FI= Fully immunized; PI= Partially immunized; NI= Non-immunized; UI= Unknown Immunization status

IV. Discussion

Diphtheria, if not diagnosed and treated promptly, can lead to significant mortality and morbidity because of its severe critical complications such as obstructive airway disease, myocarditis, polyneuritis, cranial nerve palsies, and secondary pneumonia. In the present study, all the culture positive cases presented with mild to moderate fever, sore throat, and formation of a pseudomembrane on examination. The overall culture positivity for *Corynebacterium diphtheriae* was 26.26% in the present study for the period of three years from 2013 to 2015. In a similar study carried out from 2012 to 2014, S. Bhagat *et al* from Delhi also reported persistence of *Corynebacterium diphtheriae* in Delhi and the National Capital Region (NCR), in about 23% of cases.¹² Elantamilan D *et al.*, also reported a positivity rate of 25% in a study done from NEIGRIHMS, Shillong.¹³

Diphtheria mainly affects children aged 1 year to 5 years. However, for the better vaccine coverage worldwide, a shift in the age wise incidence of the disease from pre-school to school age (5 to 15 years) has been observed with more cases now reported among adults.¹⁴ In our study also, *C. diphtheriae* positive cases were more among the patients aged 5 years and above, – 53.84% and 30.76%, respectively, in age groups 5-9 years and 10-14 years, which is similar to the study of Nandi R. *et al*¹⁵ from Assam, who reported it as 59%. A shift in age of diphtheria cases was also reported by Saikia L.*et al.*⁷ In their study of an outbreak in Dibrugarh district of Assam, they reported 100% cases to be aged >5 years. In contrast, S. Bhagat *et al*¹² reported most of their cases in 1-5 years of age. Serological studies in many countries revealed that due to lack of adult vaccination as well as natural immunity, a high proportion of adults become susceptible to diphtheria.¹⁶ The

potential for outbreaks of diphtheria in a community may be enhanced when there are susceptible adults and unimmunized children in the same community.³ Culture positivity for *C. diphtheriae* in the present study was found to be more in males (65.38%) than in female patients (34.62%). In contrast, Meera M. *et al*¹⁷ from Andhra Pradesh reported that 60% of females in their study were culture positive for *C. diphtheriae*. The higher culture positivity in our study may have been due to the fact that male children in our communities are more active than females and their contact is closer with their friends and others some of whom may be already infected or may be carriers.

The present study revealed that 62.5% of non-immunized patients were culture positive for *C. diphtheriae*. Surprisingly, 31.58% of the fully immunized patients were also culture positive. Similar to our findings, Meera M. *et al*¹⁷ also reported culture positivity among fully immunized patients (5%) in Andhra Pradesh and high culture positivity among non-immunized patients (94%).

Mild to moderate fever and sore throat were common clinical features of all of the total 99 study cases while pseudomembrane formation with mild dyspnoea were present in the 26 cases showing positive smear microscopy and culture for diphtheria. Moreover, no specific immunization status of the confirmed diphtheria cases was observed as diphtheria was confirmed in all categories of patients,– fully immunized, partially immunized and non-immunized.

V. Conclusion

The study signifies re-emergence of diphtheria in the Northeast Indian state of Assam, which calls for intensive monitoring and review of UIP implementation in the state including vaccine quality, vaccine storage and transport conditions. Enhancing effective awareness campaigns on the importance of immunization and its various benefits, both among the care providers and the communities,¹⁸ would also contribute towards an improved state.

Limitation of the study: Incomplete history of immunization of many of the study cases, which was due mainly to illiteracy and ignorance of the patients and/or their attendants; and toxigenicity tests of the *C. diphtheriae* isolates, which could not be performed due to technical reasons.

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