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SPORADIC OUTBREAK CASES OF DIPHTHERIA: A THREE YEARS' STUDY IN 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 seum 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 the 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: *Corynebacteriumdiphtheriae*, Kleb-Loeffler's bacillus, immunization, UIP and toxin.

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 close contacts, cases or carriers. 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] Data on the incidence of diphtheria are not available from some developing countries where it accounts for 80% to 90% of the global burden of diphtheria cases.[3] The incidence of the disease has also declined in India over the years because of wider vaccination coverage of the children below five years of age, with only 2,817 cases being reported in 1997.[4] In 2008, India contributed 6,081 (86.66%) of the 7,017 diphtheria cases reported globally.[5] Small outbreaks of diphtheria were reported earlier from the eastern part of Assam.[6,7]

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

MATERIALS AND METHOD

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.

Sample Collection and Processing: Two samples of throat swabs were collected from each case, one for direct microscopy and another for culture, after 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 37^0C 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.

RESULTS AND OBSERVATION

Out of the total of 99 cases, 40 in 2013, 28 in 2014 and 21 in 2015, the highest number of 35 cases were in the age group 5-9 years, followed by 25 in age group 15-45 years, 20 in 10-14 years, 16 in 0-4 years, and the lowest number of 3 in patients aged >45 years.**(Table-1).** Gender wise, there were more male cases (56) than females (43).**(Table-2).**

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 years age group.**(Table-3).**

Gender wise, *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.**(Table-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 the 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 who 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.(notshown in separatetableorchart).

Table-1. Diphtheria Study Cases : Age wise

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

Table-2. Diphtheria Study Cases : Gender wise

Year	Male	Female	Total
2013	22	18	40
2014	13	15	28
2015	21	10	31
Total	56 (56.56%)	43 43.43%)	99 (100%)

Table-3. Diphtheria Study Cases : Age and Culture Positivity

Age Group In yrs	Total Cases	Smear+ve Culture +ve	Smear+ve Culture-ve
0 - 4	*16*	*1(6.25%)* (3.84%)	
5 - 9	*35*	*14(40%)* (53.84%)	
10 - 14	*20*	*8(40%)* (30.76%)	
15 - 45	*25*	*3(12%)* (11.53%)	
>45	*3*	*0*	
Total	*99*	*26(26.26%)* (100%)	*4(4.04%)*

Table-4. Diphtheria Study Cases : Gender and Culture positivity

Gender	Total Cases	Smear+ve Culture +ve	Smear+ve Culture-ve
Male	56	17 (30.35%) (65.38%)	
Female	43	9 (20.93%) (34.62%)	
TOTAL	99	26(26.26%)	4(4.04%)

Table-5. Diphtheria Study Cases : Immunization Status and Culture positivity

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

FI=*Fullyimmunized**; **PI=** *Partially immunized*; **NI=** *Non-immunized*; **UI=** *Unknown Immunizationstatus

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.[8]

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.[6] 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* [7] from Assam, who reported it as 59%. A shift in age of diphtheria cases was also reported by Saikia L.*et al.* [9] 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*[8] 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.[10] 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%). Meera M. *et al* [11] 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* [11] 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.

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,[12] 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 some inconveniences.

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