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Re-emergence of diphtheria in Malappuram district, North Kerala, India

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Abstract:

BACKGROUND AND OBJECTIVE: An outbreak of diphtheria was identified in Malappuram district, North Kerala, India, from July 2016 onwards as a sudden increase in the number of throat swabs with suspected diphtheria received in the Microbiology Lab of Government Medical College Manjeri, Malappuram district. The objective of this study was to confirm the outbreak and identify the organisms and their antibiotic sensitivity patterns.

MATERIALS AND METHODS: A total of 554 throat swabs were received from July 2016 to June 2017 from neighbouring areas of Malappuram district for culture and sensitivity. Elek gel precipitation test and polymerase chain reaction of the isolates were performed at the State Public Health Lab, Thiruvananthapuram. All isolates of *Corynebacterium diphtheriae* possess diphtheria toxin gene. Antibiotic sensitivity tests were performed. Repeat swabs were not included in the study.

RESULTS: Of the 29 (5.23%) confirmed cases, 18 (62%) were male and 11 (38%) were female. Fourteen (48.3%) cases were between 6 and 10 years of age with nine (64%) males and five (36%) females. Seven (24.2%) were between 11 and 15 years of age with four (57%) males and three (43%) females. Three (10.3%) were between 16 and 20 years of age (all males). Two (6.9%) cases from 26 to 30 years and one (3.4%) each from 21 to 25 years, 31–35 years and 36–40 years. All isolates were Penicillin sensitive.

CONCLUSIONS AND DISCUSSION: Our study identified an upsurge of diphtheria in Malappuram district, North Kerala, among older children and adolescents. Most of them are partially immunised and immunity to diphtheria declines over time. Adults and adolescents thus become susceptible later in life. This emphasises the need for booster vaccination above five years in the endemic areas and making antidiphtheritic serum available in all major hospitals of these regions.

Keywords:

Corynebacterium diphtheria, *Corynebacterium pseudodiphtheriticum*, Diphtheria, vaccine

Introduction

Diphtheria is a rare disease in most developed countries owing to the routine childhood vaccination.[1] However, the disease is seen occasionally among non-immunised children in developing countries.[1]

Diphtheria is endemic in India; the incidence has shown a decline mainly due to widespread vaccination coverage of under-five children.[1] In developing countries, the disease continues to be endemic due to the lack of adequate immunisation coverage, waning of immunity to diphtheria in adults and movement of large group of population in the past few years.

Recent diphtheria outbreak in a number of countries including our country has demonstrated a shift in the age distribution of cases to older children and adults.[2,3] This highlights the need for booster vaccination. We report such an outbreak of diphtheria in Malappuram District, North Kerala, India.

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Materials and Methods

The Department of Microbiology, Government Medical College, Manjeri, has started receiving throat swabs from clinically suspected cases of diphtheria on 4 July 2016 onwards from patients of all age groups. Cases were determined as 'suspected' according to the interim guidelines released by the Government of Kerala.[4] Swabs sent for other reasons like follicular tonsillitis were excluded from the study.

The throat swabs were processed. Gram-staining and Loefflers methylene blue staining were performed. Culture was done on conventional media and *Corynebacterium diphtheriae* was identified using conventional methods.[5,6] Antibiotic sensitivity testing was performed using Kirby Bauer disc diffusion method on Mueller–Hinton blood agar plates.[7] All isolates were sent to State Public Health Lab, Thiruvananthapuram, for Elek gel diffusion test and Tox gene demonstration by polymerase chain reaction. The isolates were identified by amplification of specific sequences of the ToxA and ToxB genes using the primers described previously.[8]

Elek test was performed to confirm the expression of the Tox genes using the modified Elek test protocol. The test was done in 50-mm glass petri dishes with Elek test agar base supplemented with newborn calf serum. A sterile filter paper with 10 IU/ml of anti-toxin was used. The test organisms were streaked at a distance of 10 mm from the disk along with positive and negative controls. The plates were observed after 24-h incubation at 37°C. Formation of precipitin lines between the disk and the inoculum is taken as positive.[9]

Results

We have received 554 throat swabs from suspected cases of diphtheria from patients of all age groups from various areas of Malappuram district from July 2016 to June 2017. None of our patients received full immunisation against diphtheria. *C. diphtheriae* was isolated from 29 samples (5.23%). All isolates were Tox gene positive and showed line of precipitation. All were sensitive to Penicillin. Age and sex distributions of suspected and confirmed cases are shown in Table 1.

Two isolates were resistant to macrolides (Erythromycin and Azithromycin) which was further identified as *Corynebacterium pseudodiphtheriticum* by Vitek 2 compact system which were also from the age group of 6–10 years. *Corynebacterium pseudodiphtheriticum* is a common commensal of upper respiratory tract which can mimic mild diphtheria clinically and can be a challenge for treating physicians, especially in settings of a diphtheria epidemic.[10,11]

Discussion

Most of the confirmed cases belonged to the age group of 6–10 years and a substantial minority in the age group of 11–15 years, suggesting that the very young remained well protected by high rates of infant immunisation. The increased susceptibility risk in older children could be explained either by failure to undergo vaccination in early childhood or by waning immunity; the level of antibodies decreases with time and adults may again become susceptible to diphtheria due to reduced opportunities for boosting through sub-clinical infections.[12]

Decrease in antibody titres resulting in declining immunity could, in turn, be a result of absence of boosting by contact with circulating toxigenic strains of *C. diphtheriae* as well as repeat vaccination.[13] This picture of age shift has been documented in other data published from India. Another study from India showed a similar age shift of 45% of cases from children above five years.[14] Male children (18/29–62%) were more than females (11/29–38%) in confirmed cases due to the fact that in rural areas boys were more engaged in outdoor activities, thereby coming in contact with infected cases.

No confirmed cases were documented in the age below five years or above 40 years. Although immunised individuals can develop clinical diphtheria, even partial immunisation reduces morbidity and mortality rates by more than 50%.[15]

All the patients responded well to injectable Penicillin (CP 200,000 IU/kg in four divided doses for 14 days) and antidiphtheritic serum (20,000–100,000 units, half the dose being given I/V) treatment. All cases needed an average 15-day hospitalisation and were discharged after seeing the negative culture report. Two patients developed myocarditis and responded well to medical treatment.[16] Contacts were given erythromycin tablets (40 mg/kg/day in four divided doses for 14 days).

Post exposure diphtheria prophylaxis was given to all health care providers with 3 doses of Td vaccine (0-1-6 months) Most of the cases were from a particular category of people who are reluctant to take immunisation, and it was very difficult to convince them about the advantages of childhood immunisation. Therefore, public health strategies should aim for more than 90% coverage among paediatric population and strongly promote periodic adult boosters.

Successful childhood immunisation programmes are beneficial in preventing toxigenic strains from circulating in the community, among both vulnerable children and adults. Failure to implement immunisation

Table 1: Age and sex distribution of samples and isolates

Age group (years)	Male		Female		Total	
	Patients	Isolates	Patients	Isolates	Patients	Isolates
0-5	27	0	19	0	46	0
6-10	80	9	83	5	163	14
11-15	69	4	41	3	110	7
16-20	20	3	27	0	47	3
21-25	12	0	28	1	40	1
26-30	13	1	31	1	44	2
31-35	17	1	21	0	38	1
36-40	10	0	21	1	31	1
41-45	3	0	5	0	8	0
46-50	4	0	4	0	8	0
51-55	3	0	7	0	10	0
56-60	1	0	4	0	5	0
61-65	1	0	3	0	4	0
Total	260	18	294	11	554	29

Maximum number of samples and isolates were from the age group of 6–10 years

programmes can result in avoidable epidemics and causing adult disease. Data may not truly reflect the extent of diphtheria in the community due to the presence of sub-clinical and asymptomatic infections and undiagnosed cases. Clinicians should maintain a high index of suspicion while formulating a differential diagnosis in older children.

Based on our data, we conclude that diphtheria is a re-emerging vaccine preventable disease and urgent control measures and disease surveillance programmes are called for. Immunity against diphtheria depends primarily on antibody to diphtheria toxin. A high level of anti-diphtheria toxoid IgG antibody ≥1.0 IU/ml confers long-term protection and levels between 0.1 and 1 IU/ml require immediate immunisation.[12] Full protection in the highest possible proportion of the population should help to avoid re-emergence of this serious potentially fatal infectious disease.

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Conflicts of interest

There are no conflicts of interest.

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