Resurgence of diphtheria in rural north Karnataka: Clinical profile and outcome

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Abstract
Introduction: Although, diphtheria is eliminated in many developed countries by effective immunization, diphtheria still continues to be endemic in India and is the leading cause of morbidity and mortality, especially in rural parts of North Karnataka. The objective of the present study is to recognize the clinical profile, morbidity and mortality pattern of diphtheria and to study their immunization status as a hospital based observational study performed in paediatric intensive care unit.

Materials and Methods: This study is a hospital based observational study from April 2018 to August 2018 at a tertiary care referral PICU, S.Nijalingappa Medical College and HSK hospital, Bagalkot, Karnataka. The cases were analysed with respect to demographic details, clinical features, immunization status, complications and mortality.

Results: The study consisted of 22 children who presented with features suggestive of diphtheria, 90% were >5 years of age with male to female ratio of 1.2:1. Of the 22 children 4 (18.2%) children were completely immunized, and 18(81.8%) were partially immunized/not immunized. All patients presented with fever, membrane in throat and throat pain (100%) followed by bull neck 54.5%, dysphagia 36.36%, epistaxis 9% and Airway obstruction 4.54%. Alberts stain was positive in 18 cases (81.8%) and throat swab culture positive in 16 cases (72.7%). Myocarditis was the commonest complication (63.6%) followed by palatal palsy (13.63%), shock (4.5%) and stroke (4.5%). Case fatality rate was 18.18%.

Conclusion: Shifting of occurrence of diphtheria in the age group of >5 years suggest the need to improve and strengthen the immunization program specially the booster doses.

Keywords: Diphtheria, Immunization, Myocarditis, Stroke.

Introduction
Many outbreaks of diphtheria form various states in India have been reported in recent times 1-5. In 2010, India shared 3123 (77.1%) of 4053 diphtheria cases contributed by 24 countries, reported to WHO, which may possibly be a gross underestimate due to lack of a good surveillance system & facility for microbiologic diagnosis6,7. Inadequate vaccine coverage in young children, waning vaccine induced immunity in adults, mass population movements, poor living standards, delayed reporting to hospital and non-availability or delay in administering antitoxin appears to be the main factors contributing to re-emergence of the disease and high mortality8,9.

In scenario of changing epidemiology of diphtheria, studies reporting clinical profile remains scanty10. A large number of diphtheria cases are treated at our hospital. It was therefore decided to analyse the information to bring out the clinical and demographic profile of diphtheria cases and predictors of mortality. This would help in early recognition of cases and referring them timely to higher medical care facility and to prioritize intensive care, which may reduce morbidity and mortality.

Aims and Objectives
1. To study the immunization status of affected children.
2. To know the microbiological confirmation rates.
3. To identify the mortality and morbidity trends of diphtheria.

Materials and Methods
Place of study: S.Nijalingappa Medical College and HSK Hospital.

Study Population: All 22 children with clinical suspicion of diphtheria admitted in paediatric intensive care unit.

Study Period: April 2018 to August 2018.

Type of study: Observational case series study.

The case data was analysed with respect to demographic details, clinical features, immunization status, pseudo membrane, complications and mortality. The immunization status was documented as per the information given by the parents. Those who had received three primary doses at 4-6 weeks interval starting at 6 weeks of age, followed by booster doses at 18 months and 5 years were recorded as “Immunized”. Those who had not received any doses were considered as “Unimmunized”. Patients who had missed one or more of the three primary doses or booster doses were included as “Partially immunized”. All children with clinical suspicion of diphtheria were admitted in paediatric intensive care unit and started on oral erythromycin in the dose of 40 mg/kg/day in 4 divided doses. Antidiphtheritic serum (ADS) was given in a single dose (50,000 IU-1,00,000 IU) intravenously over 1 hour by proper sensitization method. Throat swab for Albert’s stain and culture were sent in all, at the time of admission.

Results
Out of 22 children, 2 patients (10%) were less than 5 years age group and 20 patients (90%) were above 5 years.
12 patients (54.54%) were males and 10 (45.45%) were females.

Morbidity and mortality
Case fatality rate: There were 4 deaths with a case fatality rate of 18.18%.

Immunization status of the affected children
Four (18.2%) were immunized fully and 18 cases (81.8%) were unimmunized/Incomplete/partial immunized.

Bull neck
Out of 22 children, 12 (54.54%) children presented with bull neck at presentation.

Myocarditis
Out of 22 children, 14 (63.63%) children developed myocarditis. Out of 14 children who developed myocarditis, 4 (18.18%) children succumbed to death.

Microbiological confirmation rates
Albert staining was performed in 22 cases of which 18 (81.8%) were positive. Culture was performed in 22 cases of which 16 were positive (72.7%).

Antidiphtheritic serum (ADS) administration:
ADS was administered in all 22 cases.

Table 1: Demographic data
| Variable            | Data       |
|---------------------|------------|
| Age                 |            |
| <5 years            | 2 (10%)    |
| 5-7 years           | 6 (30%)    |
| >7 years            | 14 (60%)   |
| Sex                 |            |
| Male                | 12         |
| Female              | 10         |
| Immunization status |            |
| Immunized           | 4          |
| Partially immunized / unimmunized | 18 |
| Contact History     |            |
| Present             | 5          |
| Absent              | 17         |

Table 2: Clinical Presentation
| Symptoms            | Data |
|---------------------|------|
| Fever               | 22   |
| Throat pain         | 22   |
| Cough               | 15   |
| Bull neck swelling  | 12   |
| Dysphagia           | 8    |
| Epistaxis           | 2    |

Table 3: Laboratory Investigations
| Lab parameter | Data |
|---------------|------|
| Albert stain  |      |

Discussion
In the pre-vaccine era, disease was common among children less than 5 years of age due to natural boost to the development and maintenance of immunity in adolescence and adults. However, after widespread immunization in children, lack of or inadequate booster doses in children and adult and decrease incidence of cutaneous diphtheria, there is shift of age for the occurrence of disease in older children and adults. Such a shifting of age of occurrence was observed in developed and developing countries including India.

In present study 90% patients were more than 5 years of age. However, Meshram et al (55.32%), Basavaraja JC et al (74.1%), Bandichhode ST et al (66.66%) were reported resurgence of disease in children more than 5 years of age.

In present study, males and females are almost equally affected giving sex ratio 1.2:1 which is almost similar to Meshram et al. Similar types of sex distribution were reported by many authors, while Mehariya et al observed male predominance below 10 years of age and few studies noted predominantly female involvement.

Most of the patients in present study from rural area and from lower socioeconomic class, could be because of our hospital mainly served to socioeconomically deprived rural population who have poor access to immunization, health care system and overcrowding. Similarly, high incidence of disease in rural and lower socioeconomic class were reported by Mehariya et al and Singh SN et al.

Though, the Expanded Programme of Immunization (1978) and Universal Immunization Programme (1985) was launched almost four decades before in aim to reduce childhood morbidity and mortality of vaccine preventable diseases by offering full immunization coverage. Present immunization coverage in India is around 61%, with wide state wise, geographical, religion, rural urban and gender variation.

Minimum immunization coverage of 90% in children and 75% in adult is required to prevent spread of diphtheria and current coverage rates in Karnataka is 62.6% which remains inadequate.
Factors contributing to the low immunization coverage include lack of awareness, misconception, avoiding immunization for trivial reasons, migration, decline in enthusiasm to routine immunization, unilateral focus on pulse polio campaign, short supply of vaccine, not maintaining proper storage of vaccine (cold chain), poor clinic organization, non-availability of immunization services on all day of week, not opening a multidose vial if enough children are not present and delaying or postponing vaccination in minor childhood illness.\(^{17}\)

In present study, 4(18.2%) patients were fully immunized, 18(81.8%) were partially immunized or unimmunized. This denotes unsatisfactory immunization coverage with DT/DPT (Diphtheria, Pertussis and Tetanus) vaccine in respective rural area. Such types of observation were reported by various authors.\(^{5,13}\) Nowadays, there are no surveillance system for vaccine preventable diseases except poliomyelitis and measles. Many authors have highlighted deteriorating health infrastructure and significant drop out between 1st and 3rd dose of DPT, because of DPT is known for adverse effect due to its pertussis component.\(^{18}\)

The clinical manifestation can vary from mild to severe to the life threatening depending on immune status of host and severity of infection. All patients presented with fever, membrane in throat and throat pain (100%) followed by bull neck 54.5%, dysphagia 36.36%, epistaxis 9% and airway obstruction 4.54%. Similar clinical details were reported by various authors from various parts of India. Cases of diphtheria were seen throughout the year but more number of cases was observed during month of June to September during rainy season. Some authors reported peak during the winter season and some in rainy season.\(^{5,13}\) In view of poor specimen collection on usual throat swab, delayed transportation to the lab, delayed inoculation to the special culture media and prior antibiotic therapy, Alberts stain was positive in 18 cases (81.8%) and throat swab culture positive in 16 cases (72.7%). But low Corynebacterium yield were reported by Basavaraja et al (16.1%),\(^{12}\) Bandichhode et al (33.33%),\(^{13}\) Singh SN et al (30.63%)\(^{15}\).

Myocarditis was the commonest complication (63.6%) followed by palatal palsy (13.63%), Shock (4.5%) and Stroke (4.5%). Case fatality rate was 18.18%. In India, incidence of diphtheric myocarditis varies from 16 to 66%.\(^{11}\)

Palatal palsy was characterized by a nasal quality of voice, nasal regurgitation commonly occurring in second and third week and is the earliest neurological complication which may occur alone or in association with other types of paralysis. However in Meshram et al study,\(^{11}\) 7(14.89%) patients had palatal palsy and 4(8.51%) had polynuropathy with or without cranial nerve involvement.

Diphtheria, if not detected early and treated late can lead to significant mortality and morbidity because of critical complication. Specific antitoxin is used without waiting for laboratory confirmation to neutralize the unbound toxin in blood.

Corynebacterium is susceptible to antimicrobials like penicillin, erythromycin, clindamycin and metronidazole. Therapy is to be given for 14 days and it is important to maintain isolation, treatment of carriers and prevent spread. Case fatality was 18.18% in our patients which is almost similar to Mesharam et al (21.28%)\(^{11}\) where as it is ranged from 9-14% in Maharashtra, 32-56.3% in different centers in north India and 23.67% in West India. Diphtheria is still not a lost entity as cases are coming to tertiary care level. Immunization activity needs to be improved and strengthened in borderline districts as most of the cases in present study were from rural areas. Present study showed complete immunization, high index of suspicion and diagnosis and early prompt administration of antitoxin prevent the complication and mortality.

**Conclusion**

Although, we have reduced the incidence of vaccine preventable diseases by vaccination, diphtheria is still a matter of concern for public health. Shifting of occurrence of disease in 5-15 years age group suggest the need for completing the immunization schedule, especially booster doses. Therefore awareness should be created at community level by anganwadi workers about booster doses and vaccination card should be made as a compulsory document for school admissions. High mortality observed with cardiac involvement and neurological complication denotes the need of early diagnosis and prompt antitoxin therapy to prevent mortality. Immunization activity needs to be improved and mop up immunization should be done in endemic rural areas.

**Conflict of Interest:** None.

**References**

1. Patel UV, Patel BH, Bhavsar BS, Dabhi HM, Doshi SK. A retrospective study of diphtheria cases, Rajkot, Gujarat. Indian J Commun Med 2004;29:161.
2. Dravid MN, Joshi SA. Resurgence of diphtheria in Malegaon and Dhule regions of north Maharashtra. Indian J Med Res 2008;127(6):616-617.
3. Sharma NC, Banavaliker JN, Ranjan R, Kumar R. Bacteriological and epidemiological characteristics of diphtheria cases in and around Delhi-a retrospective study. Indian J Med Res 2007;126(6):545-552.
4. Bitragunta S, Murhekar MV, Hustin YJ, Renumur PP, Gupta MD. Persistence of diphtheria, Hyderabad, India, 2003e2006. Emerg Infect Dis 2008;14:1144-1146.
5. Siakia L, Nath R, Saikia NJ, Choudhary G, Sarkar M. A diphtheria outbreak in Assam, India.东南亚J通GtCaliP J 2010;41: 647-652.
6. World Health Organization. Vaccines and biological. Vaccine preventable diseases. Available from: http://www.who.int/immunization_monitoring.en/global-summary. Accessed on 07.05.11.
7. Vitek C, Wenger J. Diphtheria. Bull World Health Organ. 1998;76: S129-S130.
8. Galazka A. The changing epidemiology of diphtheria in the vaccine era. J Infect Dis 2000;181:S2-S9.
9. Singhal T, Lodha R, Kapil A, Jain Y, Kabra SK. Diphtheriadown but not out. Indian Pediatr 2000;37:728-738.
10. Jayshree M, Shruthi N, Singh S. Predictors of outcome in patients with diphtheria receiving intensive care. Indian Pediatr 2006;43:236-238.
11. Meshram RM, Patil A. Clinical profile and outcome of diphtheria in central India: a retrospective observational. *Study Int J Contemp Pediatr* 2018;5(4):1600-1605.

12. Basavaraja GV, Chebbi PG, Joshi S. Resurgence of diphtheria: clinical profile and outcome - a retrospective observational study. *Int J of Contemp Pediatr* 2016;3(1):60-63.

13. Bandichhode ST, Jatti GM, Anita MS, Nandimath VA. A clinical study of diphtheria cases in a pediatric population in tertiary care hospital in western Maharashtra. *Indian J Child Health* 2016;3(3):251-253.

14. Meera M, Rajarao M. Diphtheria in Andhra Pradesh-a clinical-epidemiological study. *Int J Infect Dis* 2014;19:74-78.

15. Singh SN, Singh A, Chandra S. Clinical profile and prediction of poor outcome of hospitalized diphtheria cases in children from Lucknow region of North India. *Clin Epidemiol Glob Health* 2014;2:75-9.

16. Begg N. Diphtheria-manual for the management and control of diphtheria in the European region. WHO Publication, Copenhagen, 1994.

17. Bairwa M, Rajput M, Sachdeva S. Modified Kuppuswamy’s Socioeconomic scale: Social researcher should include updated income criteria, 2012. *Indian J Community Med* 2013;38(3):185-186.

18. Maheriya KM, Pathak GH, Chauhan AV, Mehariya MK, Agrawal PC. Clinical and epidemiological profile of diphtheria in tertiary care hospital. *Gujarat med J* 2014;89(2):105-108.

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