Diphtheria in Children- Are we even close to control the menace?

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Abstract

Introduction: Despite the success of mass immunization in many countries worldwide, diphtheria continues to play a major role as a lethal resurgent infectious disease. The case reports of resurgence/persistence of diphtheria in India represent only the tip of the iceberg.

Aims and Objectives: To study the epidemiology, clinical profile, complications and outcome of diphtheria in children.

Materials and Method: A retrospective observational study conducted at a teaching hospital. Review of case notes of all children aged 1 month – 14 years, clinically/microbiologically diagnosed and managed as diphtheria was done. Demographic, clinical & immunization status details, complications and outcome were recorded.

Results: A total of 149 cases were reviewed. Male to female ratio was 1.26:1. Maximum (65.77%) cases were reported from regions of Karnataka. Incidence of diphtheria was 0.4%. Highest incidence (46.98%) was seen in children of 5-10 years age group. Majority (69.80%) were unimmunized. Difficulty swallowing (89.93%) and bull neck (81.21%) were common presentations. A total of 79 complications were seen of which myocarditis was the commonest (41.77%). Of 149, 98 (65.77%) recovered and were successfully discharged. CFR was 29.53%. Maximum deaths (50%) were seen in 1-5 year age group. Most children (88.63%) died within 5 days of hospitalisation.

Conclusion: Even after more than 3 decades of UIP implementation, diphtheria is still not a lost entity. A shift in age incidence was observed. Occurrence in completely immunized children points towards waning immunity with age or flaws in immunization. Uniformity and improvement in vaccine coverage, adolescent/adult immunization and early diagnosis and treatment might take us closer to achieve control.

Keywords: Diphtheria, Vaccine preventable diseases, Resurgence, DTP3.

Introduction

Diphtheria is a potentially fatal, acute infectious, vaccine preventable disease of the upper respiratory system, caused by toxigenic strains of Corynebacterium diphtheriae. It is usually associated with characteristic leather like adherent pseudo-membrane at the site of infection. The diphtheria toxin, a protein, can cause myocarditis, polyneuropathy and other systemic toxic effects. It was a leading cause of childhood mortality in pre vaccination era.[(1)] The disease has been almost completely eradicated in many developed countries. On the contrary, in developing countries, although the incidence has reduced, it still accounts for 80-90% of global burden.[(2)] In 2016, India reported 50.17% (3380/6736) of the globally reported cases of diphtheria.[(3)] There have been reports of outbreaks/epidemics from Assam (2010),[(4)] Karnataka (2011)[(5)] and Andhra Pradesh (2014)[(6)] among other Indian states. There have been case reports from developed nations also, with some cases in adults, for example - Australia (2011) – fatal diphtheria in a young woman, Spain (2015) – 6 year old unvaccinated child, Belgium (2016)[(7)] – fatal case in an unvaccinated child, to name a few.

Despite success of mass immunization worldwide, it remains a lethal resurgent infection. However, reports of resurgence/persistence of diphtheria represent the tip of the iceberg as not all cases are not reported or published. There is no system for surveillance of diphtheria in India. Thus, diphtheria is widely prevalent but neglected from a public health perspective.

An accurate microbiological diagnosis of diphtheria is crucial and is always regarded as being complementary to clinical diagnosis, because diphtheria is often confused with other conditions such as severe streptococcal sore throat, Vincent's angina of glandular fever.[(8)] This makes a high index of suspicion mandatory for diagnosis of diphtheria. Early diagnosis and timely intervention help to reduce incidence, contain infection in the community and decrease morbidity and mortality in affected individuals.[(9)]

Solapur serves as catchment area for diphtheria cases from Solapur itself and bordering districts of Karnataka and Maharashtra. There has been regular influx of diphtheria cases over the years and so it was pertinent to study these cases**.** The aim of this study was to assess incidence, presentation and complications of disease, the immunisation status of cases and treatment outcomes.

Materials and Method

This study was based on a retrospective analysis of the available records of diphtheria cases diagnosed clinically / microbiologically and admitted to Pediatric ward of Dr. V.M. Government Medical College, Solapur from January 2008 to December 2016. Demographic details, immunisation status, clinical presentation/features, complications and outcome of the

cases were noted. Immunisation status was documented as per information provided by parents. Those who received 3 primary doses of DTP vaccine at 4-6 weeks interval starting at 6 weeks age, followed by booster doses at 18 months and 5 years were recorded as completely immunised. Those who had not received any dose were considered unimmunised. Patients who had missed 1 or more dose of the 3 primary doses or booster doses were included as partially immunised.[10] It was noted from the records that throat swab for Gram and Albert's stain and culture studies were sent in all patients at the time of admission. All patients were given appropriate antibiotics. Anti-diphtheritic serum (ADS) was given to 122 children, based on its availability and affordability of patient. Patients were isolated and chemoprophylaxis (erythromycin) was given to close contacts. Patients with anticipated / established complications were shifted to PICU for monitoring and management. Outcome of patients was recorded.

Results

There were a total of 149 cases of diphtheria admitted in the period from January 2008 to December 2016. This comprised of 0.40% of the total admissions. Of these, 55.70% were males and 44.30% were females. M:F ratio was 1.26:1. Majority of these patients (65.77%) of diphtheria were residents of Karnataka, while rest were from urban and rural parts of Solapur. Of the 98 cases from Karnataka, majority (45.92%) were from the district of Gulbarga. Maximum number of cases were reported in the year 2009 (29) and least in the year 2015 (4), with clustering of cases (67.79%) in the months of July-December.

Age wise distribution of cases: Maximum patients (46.98%) were in the 5 – 10 year age group followed by those in 1-5 year age group (40.94%). The youngest patient was 11 month old unimmunised male child who had history of contact with a case in neighbourhood. Sixteen (10.74%) patients were above the age of 10 years, oldest being 13 year old unimmunised female child.

Immunisation status of the patients: Only 11 out of the 149 (7.38%) cases were completely immunised, while close to 70% (104/149) were unimmunised. Rest of the patients (34/149) had missed ≥ 1 primary dose or booster dose. Amongst patients more than 10 years old, 12 were unimmunised, 1 was partially immunised and 3 were completely immunised.

Presenting complaints: Difficulty swallowing was the most common presenting complaint of the patients, followed by bull neck swelling.

Table 1: Clinical presentation of cases

Clinical presentation	n	%
Fever	108	72.48
Cough	112	75.17
Throat pain	108	72.48
Bull neck swelling	121	81.21
Breathing difficulty	38	25.50
Difficulty swallowing	134	89.93
Change of voice	20	13.42
Bloody nasal discharge	10	6.71
Palatal palsy	07	4.70

Site of pseudo-membrane: Majority patients (40.27%) had the characteristic grey white dirty adherent membrane over the fauces followed by membrane over tonsil/s in 23.49%. Pseudo membrane covering the tonsils, post pharyngeal wall, uvula a well as the palate was present in 18.79% of the patients. The rest of the patients had membrane either over the nasal cavity (4.02%), posterior pharyngeal wall (8.05%), larynx (2.01%), nasopharynx (2.68%) and palate (0.67%).

Microbiological confirmation rates: Of the 149 swabs taken, 101 were positive for Albert's stain and 107 had growth of C. diphtheriae on culture. However in only 75 cases (50.33%), both swab and culture were positive for Corynebacterium diphtheriae. The yield of the throat swab was 67.78% and that of culture studies as 71.81%.

Complications: A total of 79 complications were observed amongst the 149 cases. Of these, myocarditis was the commonest complication to occur, seen in 22.14% cases. It presented as cardiogenic shock, palpitations, tachycardia, prolonged QTc interval, heart block, ST-T changes on ECG, muffled quality of heart sound on auscultation, falling / low ejection fraction on echocardiography.

Table 2: Complications observed

Complication	n	%
Myocarditis	33	22.14
Disseminated Intravascular Coagulation	10	6.71
Polyneuropathy	08	5.37
Aspiration	09	6.04
Septic shock	05	3.36
Airway obstruction	07	4.70
Respiratory failure	07	4.70

Outcome: Among the 149 cases, 98 (65.77%) recovered and were subsequently discharged. Forty four patients died, Case Fatality Rate being 29.53%. Half of these deaths occurred in children of 1-5 year age group. All patients who died were either partially or completely unimmunised and had developed 1 or more complication/s. Most of the patients (88.63%) died within 5 days of hospitalisation. Out of these 39

patients, 15 died within 24 hours of hospitalisation. Of the 122 patients who received ADS, 22 died.

Six patients (4.02%) were discharged against medical advice for social, personal or financial reasons. One patient with complete heart block secondary to myocarditis was referred to higher centre for pacemaker implantation.

Discussion

With the advent of expanded programme on immunisation (EPI) in 1978 and universal immunisation programme (UIP) in 1985, most of the vaccine preventable diseases have shown a decline but diphtheria is still endemic in our country.[11] In the last 10 years, there have been number of reports of either re-emergence or persistence of diphtheria from several Indian states, including Andhra Pradesh, Delhi, Maharashtra, Chandigarh, Gujarat, Assam, West Bengal, Madhya Pradesh, Uttar Pradesh, Rajasthan and Haryana.[11,12-21] India accounted for 19-84% of the global burden from 1998-2008. In 2014, India accounted for 83.24% (6094/7321) of the globally reported cases of Diphtheria. In 2016, India reported 50.17% (3380/6736) of the globally reported cases of diphtheria.[22]

Among all vaccines, diphtheria toxoid is one of the most effective and safest. India should have controlled diphtheria to such low levels that it should have been rare in this century. Therefore resurgence of diphtheria is quite disturbing.

Despite improvement in DTP3 coverage from 70% in 2008 to 87% in 2016, cases of diphtheria continue to occur.[23] Minimum immunisation coverage of 90% in children is required to prevent spread of diphtheria.[24] Poor routine immunisation as observed in our study is consistent with poor routine immunisation status in the state and the country. This corroborates with findings of other studies by Kole AK et al,[25] Kumar R et al[26] and Maheriya KM et al,[10] who also reported majority of their cases as being unimmunised. As per the NFHS-4 (2015-16), the coverage of DTP3 has been 77.9% (urban 72.7% & rural 82.1) in Karnataka whereas that in Maharashtra it was 74.9% (urban 75% & rural 74.8%). The differential rates of immunisation coverage among the rural and urban parts of a state and the neighbouring state pose a threat for spread owing to the easy travel and migration of people.

Diphtheria mainly affects children aged between 1-5 years, however, a shift in the age incidence has been observed, as in this study, from preschool to school age (5-15 years). This may be attributed to waning immunity as the child grows up and poor immunisation coverage rates with 3 doses of DTP and subsequent boosters.

The presenting complaints in our study were same as those associated with infection of the upper respiratory tract. Other studies by Kole AK et al,[25] Kumar R et al[26] and Maheriya KM et al[10] also observed sore throat, fever and swallowing difficulty as the common presenting complaints. A high index of suspicion is thus necessary for early diagnosis and treatment. Late diagnosis and treatment may predispose the patients to life threatening complications and even death.

Case fatality rate (CFR) in present study was 29.53%, which was higher than that observed by Meera M et al[6] (21.23%) and Maheriya KM et al[10] (23.68%) whereas lower than that reported by Basavaraja V et al[27] (41%). CFR ranged from 32% to 56.3% in different centres in North India and 42.9% in West India.[11,15-16] Maximum deaths in our study were within 5 days of hospitalisation. This may be due to delayed presentation to the hospital and/or presence of complications at the time of hospitalisation.

Anti-diphtheritic serum was given to 122 patients in our study. The prime reasons for it being not given to rest were unavailability of ADS and unaffordability on the part of the patient. Of those who did not receive ADS, 81.48% died. High mortality was recorded in another report from India in which CFR was 30.8% during an outbreak. None of the patients benefitted from antitoxin since none was available.[28]

Conclusion

Even after more than 3 decades of UIP implementation diphtheria remains an important vaccine preventable disease with high case fatality. Cases and mortality reported are not a true reflection of community figures as it was a hospital based study. A shift in the age incidence of diphtheria is observed. Improving and achieving uniform vaccination coverage, high index of suspicion for early diagnosis and treatment and uninterrupted supply of antitoxin may help us achieve control and reduce CFR of diphtheria. Occurrence of cases in adolescents / adults may reflect waning immunity and necessitate booster doses at that age.

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