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Original Research Article

The outcome of resurgence of diphtheria in older children in a tertiary care hospital

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ABSTRACT

Background: Diphtheria is a fatal bacterial infection which affects the mucous membranes of oropharyngeal and nasal cavity, caused by aerobic gram-positive bacteria Corynebacterium diphtheriae. With the advent of universal immunization against diphtheria the incidence of this infectious disease has declined dramatically with few developed nations having eradicated the disease. No large outbreaks have been reported in India in recent times.
Methods: In present study, authors reviewed an outbreak of diphtheria in Davangere between the months of June 2017 and July 2018. Case records of children suspected to have diphtheria, admitted to hospitals affiliated to JJM Medical College, Davangere were retrospectively analysed.
Results: 15 cases were suspected to have diphtheria on clinical examination. The mean age of presentation was 7.5 years. Fever, sore throat, difficulty in swallowing, neck swelling and patch in oral cavity were the common signs and symptoms. Airway compromise, myocarditis and neurological complications were noted. Antidiphtheritic serum (ADS) was tried in all 15 cases. Case fatality rate was 40%.
Conclusions: Diphtheria is a resurgent problem in India. Prompt identification and early appropriate treatment is essential to prevent morbidity and mortality. Strict adherence to the national immunisation schedule should also be emphasized.

Keywords: Antidiphtheritic serum, *Corynebacterium diphtheriae*, Gram positive, Myocarditis

INTRODUCTION

Diphtheria is an infectious disease caused by the exotoxin produced by *Corynebacterium diphtheriae*.[1] The organisms are locally invasive and secrete exotoxins which leads to myocarditis, paralysis and death. Despite the success of mass immunization in many countries worldwide, diphtheria recently been enjoying a minor resurgence due to waning immunity and inadequate coverage with booster vaccination, has led to the epidemiologic shift in the vulnerable age group to adolescents and young adults. This review aims to revisit the diphtheria infection and analyze the factors behind the resurgence of the it in recent years.

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, or glandular fever.[2]

Detection of the lethal and potent exotoxin produced by the causative organism is considered to be the definitive test for the diagnosis of toxigenic *C. diphtheriae*.

Early diagnosis and timely intervention reduce the incidence of the disease and controls the infection in the community and decreasing morbidity and mortality in the affected individuals.[3,4]

As per world health organization (WHO) data from 2000 to 2016, over 82% of diphtheria cases occurred in children above 5 years and over 40% occurred in individuals over 15 years of age.[5] This second shift is due to the waning immunity as the child grows older and is the reason why regular booster doses are recommended. India has the maximum number of diphtheria cases in the world, from 2011 to 2015 India had a total of 18,350 cases of diphtheria.[6] Over 40% of cases reported in India are from individuals over 15 years and about 20% cases are reported from children under the age of 5 years.[7] The aim of this study is to assess the clinical profile, laboratory diagnosis and relationship between clinical diphtheria with immunization status.

METHODS

This retrospective study was conducted in the months of June 2017 and July 2018 in JJM Medical College, Davangere.

Inclusion criteria

- A total of 15 patients aged between 1 and 15 years of age presenting with clinical suspicion of diphtheria were included in the study.

After taking informed consent, a pre-structured proforma was used to record the relevant information from individual cases selected for study, detailed clinical examination was conducted. Immunization status was documented as per the information given by the parents. Under aseptic precautions, two throat swabs were taken from all suspected cases of diphtheria. Throat swabs were smeared on nutrient agar, Mc conkey agar and Loeffler's serum slope. Then cultured colonies were stained with Gram's stain and Albert stain. All the patients registered under the study were given appropriate antibiotics and antidiphtheritic serum (ADS).

RESULTS

There were 15 suspected cases of diphtheria admitted to JJM medical college, Davangere from June 2017 to July 2018.The medical records of the cases registered under this study were analyzed retrospectively. The cases in this study belong to age group of 1-15 years of age. The mean age of presentation with clinical suspicion of diphtheria is 7.5 years. Out of 15 cases, 10 cases were males (66.6%) and 5 cases were females (33.3%). The number of cases between 1-5 years of age is 1 case (6.6%), 6-10 years of age are 10 cases (66.6%) and 11-15 years of age are 4 cases (26.6%). In presentstudy group the maximum cases of resurgence is seen in the age group between 6-10 years (i.e. 10 cases 66.6%). Fever and pain (100%) and swelling in the neck (77.7%) were the most common complaints. A tonsillar patch was noted in 100% of the cases. Microbiologically confirmed cases (Culture and staining) of *C. diphtheriae* were 6 cases (40%). Out of 15 cases, 15 cases had pharyngeal or faucial patch (100%), 4 had laryngeal involvement (26.6%) and 1 had nasal involvement (11.1%).

Figure 1: Bull neck appearance.

All patients received anti-diphtheritic serum, between 20,000 to 1,00,000 units intravenously, depending on clinical severity. Intravenous antibiotics (i.e. penicillin usually and erythromycin in patients allergic to penicillin) were routinely administered. Out of 15 cases, 10 cases (66.6%) got partial immunization with primary dose alone and 5 cases (55.5%) are unimmunized. Out of 15 patients admitted with diphtheria, 9 cases (60%) got recovered and were discharged. The remaining 6 cases (40%) succumb to death.

Figure 2: White patch over faucial pillar.

The case fatality rate was 40%. Most of the deaths occurred in patients aged between 5-10 years. Toxin mediated manifestations are important causes of mortality in settings where effective airway management is possible.

DISCUSSION

Diphtheria is an acute, highly infectious, vaccine preventable and previously an endemic disease whose

etiologic agent is *Corynebacterium diphtheriae*. Diphtheria may manifest as an upper respiratory tract infection (pseudo membrane), a cutaneous infection or as an asymptomatic carrier state. Prior to the introduction of effective vaccination, diphtheria was a major cause of morbidity and mortality worldwide, particularly among children. Exotoxin production is dependent on the presence of a lysogenic β-phage, which carries the gene encoding the toxin (tox+).[8] The toxin acts by inhibiting protein synthesis by combining with NAD+. The toxin released is absorbed into the circulation subsequently causing other organ damage mainly myocarditis, descending paralysis and ultimately death. It is spread by droplet infection from acute cases as well as asymptomatic carriers, where later being instrumental in transmission of diphtheria as much as clinical cases. With the introduction of immunization, the disease has been completely eradicated from certain western countries. The vaccine against diphtheria is given at the second, third and four months, four to five years and 15 to 18 years of age (National immunization schedule).[9] To detect the presence of active antibodies to diphtheria blood samples can be tested for serum antitoxin levels (a level of >0.1IU/ml is accepted as adequate).The diphtheria toxin is the primary virulence factor and studies have shown that the toxin is highly conserved at the amino acid level indicating that the diphtheria toxoid used for immunization is both specific to *C. diphtheria* and highly effective. The developing world is yet to achieve full immunization cover of the population and this has translated into the disease being reported in high numbers. As the number of immunized children is very small in this part of the developing world as shown in our series (un-immunized 33.3% in present study).

Reasons for poor immunization coverage in India[10]

- A short supply of vaccines, poor logistical organization
- Poor screening facilities and postponing vaccination because of minor childhood illnesses
- Widespread illiteracy and low awareness about the utility of vaccination and vaccine preventable diseases
- Ignorance about the total doses required
- Improper or absent counselling
- Vaccine side-effects
- Migration of families
- Lack of effective surveillance system for diphtheria.

Therefore, authors can emphasize the fact that there is an urgent requirement for resources to address the issue for proper immunization cover in countries such as india in order to increase them herd immunity more than 90% of the population and prevent outbreaks of the disease.

In present study authors analyzed all the cases of diphtheria hospitalized in JJM Medical College in a period of from June 2017 to July 2018. Data collected showed mean age of affected is 7.5 years. In present study, 15 cases (100%) were found to have a pseudo membrane. Authors consider a pharyngeal membrane that is difficult to peel off and leaves a bleeding area on the mucous membrane after an attempt to remove it pathognomonic for diphtheria. Our cases had 100% pharyngeal form, 26.6% laryngeal form and 6.6% nasal form of diphtheritic presentation. All patients were treated with anti-diphtheritic serum as recommended by WHO and UNICEF. The most commonly administered antibiotics were penicillin or erythromycin following recommendations of the WHO and UNICEF. Every patient in present study had a throat swab taken and 40% of cases had microbiologically confirmed disease. There was 40% mortality in present study. This observation suggests that complete vaccination is essential in preventing fatalities. Present study shows that the clinical features of the disease amongst the unvaccinated patients were similar to those observed and reported in the pre-vaccination era. Despite the shift to an older age group among diphtheria patients, this remains a potentially fatal disease with patients presenting with sore throat and respiratory distress. The coverage with DTP vaccination against diphtheria with 3 doses of diphtheria, tetanus, whole cell pertussis (DTWP) vaccine in India has been found to be over 78%. However, only about 41% of these children receive a booster dose between 18-23 months.[11]

CONCLUSION

Childhood immunization programme, especially follow up and administration of booster doses, must be prioritized. In view of the high case fatality rate and the high incidence of severe complications, it is imperative that high levels of immunity are maintained in the community through primary as well as booster immunization to prevent a resurgence of diphtheria. A high degree of suspicion and early initiation of appropriate management as well as close monitoring for development of complications are key factors in successful management of individual cases. The antigen content of the current diphtheria vaccines, especially the low antigen content of the booster vaccines, must be evaluated. Based on present study and a review of the literature, the immunization coverage against diphtheria is far from satisfactory in India. Therefore, serious efforts have to be made to increase immunization coverage and good surveillance systems ought to be put into place to enable optimum reporting of disease.

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