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Diphtheria—the patch remains

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Abstract

Background: Diphtheria, a leading cause of childhood mortality in the pre-vaccination era, has witnessed a resurgence in the last decade in the developing world and in parts of Europe. Faucial diphtheria can mimic acute tonsillitis and glandular fever, and a degree of clinical suspicion is required in order to diagnose and treat a potentially life-threatening condition. This assumes greater significance in today's world. *Objective*: To review the number of diphtheria cases admitted to Silchar Medical College and Hospital, a teaching hospital in the state of Assam in India over the last 5 years and to compare the profile of patients admitted here to cases reported elsewhere in the country and abroad. *Methods*: Details of patients were obtained from the hospital database. Comparisons were made with disease patterns reported elsewhere in the country and in parts of Europe in the late 1980s and 1990s. *Results*: A total of 101 patients were admitted with diphtheria over a period of 5 years (March 1997–March 2002). There were no peaks in the incident rate. About 82% of the patients admitted were below the age of 15. One adult with microbiologically confirmed diphtheria was seen. Immunisation status varied between no cover (70%), incomplete immunisation (20%), and full immunisation (10%). A majority of patients were from the rural environment and were economically disadvantaged. Treatment involved the administration of anti-diphtheritic serum (diphtheria antitoxin), IV Penicillin, and where indicated, tracheostomy. *Conclusions*: Results obtained show an endemic pattern of the disease in this part of the world. Persistence of the disease is due to poor immunisation coverage and problems such as poor hygiene associated with poverty. There is a rural preponderance of cases as opposed to the epidemics reported elsewhere in the country, the newly independent states of the former Soviet Union, and in parts of the USA. The case of the adult points to an interesting change in the normal age distribution of the disease.

Keywords: Diphtheria; Immunisation; Epidemics

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1. Introduction

Diphtheria has been a scourge on the horizon of human illness for thousands of years. Known since the times of Hippocrates, the first epidemics were effectively described in the 6th century by Aetius. Bretonneau first called the malaise 'diphtherie' in 1826 after the Greek for a skin or hide which aptly describes the pathognomonic pseudomembrane associated with the disease.

Diphtheria is described as a consequence of infection of the mucous membrane or skin of human beings by *Corynebacterium diphtheriae*. This Gram-positive bacillus was described independently by Klebs in 1883 and Loeffler in 1884 who also mentioned its pathogenecity. The clinical effects are the result of the characteristic exotoxin produced by the bacillus which is absorbed both at the site of inoculation of the bacillus and in the blood stream and causes cellular damage and death by interfering with normal protein synthesis. Three biotypes of the bacillus are recognized—Gravis, Intermedius, and Mitis—with most infections attributed to the Gravis and Intermedius biotypes.

The disease has witnessed a resurgence in the last decade in Eastern Europe and other parts of the developed world. With the low immunisation cover still prevailing in much of the developing world, the potential for further spread exists.

We reviewed cases of diphtheria admitted to a teaching hospital in the state of Assam in India over the last 5 years in an effort to establish prevalence of the disease, methods of treatment, and outcome. We also attempted to compare the incidence of this disease in this remote part of the world with incidence reported elsewhere in the country and abroad.

The aim of this undertaking is to try and increase awareness of this dreaded disease, which is witnessing a resurgence. This is especially important in today's world.

2. Methods

A retrospective study was conducted in a teaching hospital in the state of Assam in India of cases of diphtheria admitted between March 1997 and March 2002. Information pertaining to the age, sex, immunisation status, clinical features at presentation, length of hospital stay, and the outcome of treatment was obtained from the clinical records.

For the purpose of the study, a case of diphtheria was defined as a patient with a sore throat and a pharyngeal membrane diagnosed as diphtheria by a physician or a patient with catarrhal symptoms (sore throat without a membrane and a culture positive for *C. diphtheriae*) [1,2]. The severity of diphtheria cases were defined according to WHO criteria [3]. The form is determined by the extent of the membrane. The 'catarrhal' variety describes erythema of the pharynx without membrane but with culture positive for *C. diphtheriae*. 'Follicular' variety presents with patches of exudates over the pharynx and tonsils. 'Spreading' variety describes a membrane covering tonsils and posterior pharynx. In 'combined' cases, there are usually two anatomical sites involved, i.e., throat and skin.

Data gathered were analysed by using simple statistical methods.

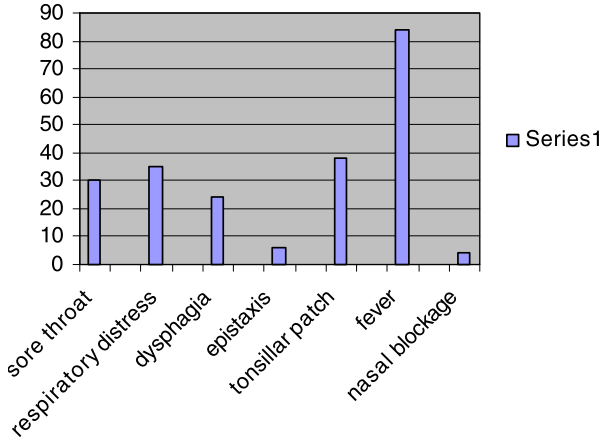

Fig. 1. Clinical presentations.

3. Results

There were 101 cases of diphtheria admitted to the hospital in the 5-year period between March 1997 and March 2002. All these patients met inclusion criteria for the study. The medical records were analysed retrospectively.

There were 46 female patients. Only 30% of the patients had prior vaccination. Patients less than 5 years old were 41% of the cases in our study. Children between the ages of 6 and 10 constituted 30% and 12% of patients were between 11 and 15 years old. Those over 15 years of age made up the remaining 18%.

Fever and sore throat were the most common complaints, 84% and 30%, respectively. Tonsillar patch was noted in 38% of the cases as shown in Fig. 1, and 65% of the cases were microbiologically confirmed cases of *C. diphtheriae*.

Most patients had pharyngeal or faucial diphtheria (90%), 5% had laryngeal diphtheria, and 5% had nasal diphtheria, as shown in Fig. 2.

Every patient received anti-diphtheritic serum, between 20,000 and 100,000 U intravenously, depending on clinical severity. Intravenous antibiotics (IV penicillin usually and erythromycin in patients allergic to penicillin) were routinely administered. Dexamethasone was administered in 81% of patients in order to reduce inflammation and the toxicity of the disease.

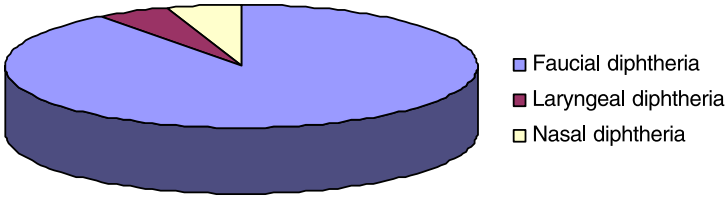

Fig. 2. Types of diphtheria.

Among 101 patients admitted with diphtheria, 75% of the patients recovered and were discharged. Patients who left the hospital with some residual complaints constituted 5% and 4% left hospital against medical advice. The mortality rate was 16%. Six patients died within 24 h of admission. Most of the deaths occurred in patients less than 4 years of age. The cause of death was noted as respiratory failure. Cardiac failure due to myocarditis was also noted.

4. Discussion

Diphtheria is an acute communicable disease produced by a Gram-positive exotoxin-producing bacillus, *C. diphtheriae*. It usually localises in the upper respiratory tract causing ulceration of the mucosa followed by formation of an inflammatory pseudomembrane. The toxin released is absorbed into the circulation subsequently, causing other organ damage and ultimately death. It is usually transmitted by means of direct contact or droplets [4]. Non-immune children below the age of 5 are commonly affected [5].

With the introduction of immunisation, the disease has been completely eradicated from certain western countries. Only 41 cases were reported in the United States during 1980 and 1985 [6]. With the advent of immunisation, demography has shifted to the adult population [7,8]. The developing world is yet to achieve full immunisation cover of the population, and this has translated into the disease being reported in high numbers. As the number of immunised children is very small in this part of the developing world as shown in our series (non-immunised 70% in our cohort), the disease was very common in both children and young adults [7].

There are also reports of the resurgence of diphtheria in both developed and developing countries like the former states of the Soviet Union [9]. The incidence of diphtheria probably is on slight decline in India, with only 1336 cases being reported in 1997 [10]. The figures quoted may possibly be a gross underestimate because of the lack of a good surveillance system. A recent series of 606 cases over a period of 5 years (1989–1983) was reported from the state of West Bengal where most of the diagnoses were clinical, with only 7% cases being confirmed microbiologically [11]. Disparity in the reported incidence of the disease in various parts of India has been attributed to variabilities in the rate of immunisation and equally importantly, lack of uniform recording and reporting procedures. As Singhal et al. reported in the *Indian Pediatric Journal*, the percentage coverage with three doses of the ‘triple vaccine’ of DPT (Diphtheria Pertussis and Tetanus) varied between 27% and 88.5% in different states of the country [9]. The survey also reported a significant drop-out rate between the administration of the first and second doses of the DPT vaccine of 22%. Details of booster doses DPT vaccines were not available [12–14].

The data thus presented is very heterogeneous, but allows some general conclusions:

1. Vaccine coverage varies widely throughout the country with significant urban and rural differences.
2. There are some independent surveys, which estimate coverage to be significantly lower than official claims. This is also shown in our study (immunisation coverage of only 30%).

3. There is a significant drop-out rate between the administration of the first and second doses of DPT.
4. Administration of booster doses of the vaccine in those previously vaccinated was extremely low.

Reasons for poor immunisation coverage in India are a short supply of vaccines, poor logistical organisation, poor screening facilities, and postponing vaccination because of minor childhood illnesses [15,16]. This is also compounded by widespread illiteracy and low awareness about the utility of vaccination and vaccine-preventable diseases [15,16]. Other factors are ignorance about the total doses required, improper or absent counselling, vaccine side effects, and migration of families. Therefore, we can emphasize the fact that there is an urgent requirement for resources to address the issue of proper immunisation cover in countries such as India in order to increase the herd immunity of the population and prevent outbreaks of the disease.

Herd immunity in populations with good immunisation cover has prevented outbreaks of the disease. A need for routine immunisation of adults in these populations (as in the former Soviet Union) is debated [17]. However, if there is a drop in childhood immunisation, an epidemic may be triggered as was seen in the newly independent state of the former Soviet Union. Therefore, routine immunisation of adults with low-strength booster doses is considered appropriate by many people [18].

In our study, we analysed all the cases of diphtheria hospitalised in a teaching institute in eastern India over a period of 5 years. Data collected shows that children as well as young adults were affected, with one case being reported in a person of 33 years age. This indicates a lack of herd immunity in the population. The sex difference was not as marked as that reported in the Russian Federation [2].

The clinical characteristics of diphtheria among the hospitalised patients in our study reflect a larger incidence of the catarrhal form (without membrane)—62%. In our study, 38% of patients were found to have a pseudomembrane.

There were few cases of laryngeal diphtheria in our study (5%). Another 5% had nasal involvement, and the remainder of cases in our study had pharyngeal diphtheria.

An interesting shift in the age distribution of the disease is noted with 18% of patients seen in the age group of 15 or more (there being also an adult male of 33 years age). Lack of herd immunity in the population studied with no evidence of booster vaccination doses are thought to be responsible for the disease occurring in adolescents and young adults [9].

All patients were treated with anti diphtheritic serum as recommended by WHO and UNICEF [19]. Most commonly administered antibiotics were penicillin or erythromycin following recommendations of the WHO and UNICEF [19,20].

Every patient in our study had a throat swab taken, and 65% of patients had microbiologically confirmed disease.

There was a 16% mortality in our study. This is comparable to other studies in literature, i.e., 3–23% [21]. Only three patients who died were recorded to have had a full course of immunisation, and their deaths can be deemed to have been due to immunisation failure. This observation suggests that complete vaccination is essential in preventing fatalities. Our 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.

5. Conclusion

Based on our study and a review of the literature, the immunisation coverage against diphtheria is far from satisfactory in India. Therefore, serious efforts have to be made to increase immunisation coverage, and good surveillance systems ought to be put into place to enable optimum reporting of disease.

There remains a risk of the disease being introduced into areas of the world where it is now nonexistent by the simple method of a carrier of the bacillus travelling long distances in today's world.

Age-appropriate immunisation, early diagnosis, full treatment of cases with anti-diphtheritic serum and antibiotics (penicillin or erythromycin), and chemoprophylaxis of close contacts of cases remain the cornerstones of effective prevention and treatment.

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