



OCCURRENCE, CLINICODEMOGRAPHIC PROFILE AND TREATMENT OUTCOME OF DIPHTHERIA CASES ATTENDING GAUHATI MEDICAL COLLEGE & HOSPITAL

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ABSTRACT

Diphtheria is a potentially fatal, acute infectious and vaccine preventable disease caused by *Corynebacterium diphtheriae*. We have taken up the study with the objective - i) to analyse the demographic distribution of cases & identify the areas for sensitization and immunization, ii) to evaluate clinical presentation & treatment outcome of cases.

Methods: All patients of diphtheria attending Department of ENT, GMCH from January 2019 to October 2020 are taken into account & data analysed regarding age, residential address, immunization status, signs & symptoms, any complications developed. Patients in the age group 0-25 years with only positive KLB staining & culture were included in study. Outcome of treatment recorded as recovered or death.

Results: Out of total 24 cases 54.16% were from 10- 25 years of age & 62.5% cases were incompletely vaccinated or unimmunized. Almost all patients presented with febrile illness, throat pain & typical pseudomembrane. Complications noted were myocarditis (54.16%) followed by cardiogenic shock, acute renal failure & airway compromise. After receiving specific treatment like benzathine penicillin, erythromycin, ADS etc. 16 patients (72.7%) recovered & 6 patients (27.3%) succumbed to death.

KEYWORDS

Diphtheria, Immunization, Clinicodemographic distribution, Treatment outcome, Fatality

INTRODUCTION:

Diphtheria is a communicable localized disease of mucous membrane or skin caused by toxigenic strains of *Corynebacterium diphtheriae*. It is a potentially fatal, acute, infectious and vaccine preventable disease of the upper respiratory system. Diphtheria was one of the leading cause of childhood death in the pre-vaccine era.¹ After invention of the diphtheria toxoid vaccine in 1923, incidence of diphtheria quickly declined in developed nations. But India is still bearing a major burden of diphtheria cases worldwide. Even after tremendous national immunization programmes, cases with *C. diphtheriae* infections still coming from remote areas, indicating poor immunization coverage in some areas of our state. In 2010, India shared 3123 cases (77.1%) of total 4053 diphtheria cases contributed by 24 countries, as reported to WHO.² Factors contributing to re-emergence of the disease and high mortality may be 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.^{3,4} Patterns of epidemiology of the disease have changed over time due to introduction of vaccination as well as changing socioeconomic conditions in countries. Prior to vaccine introduction at least 40% of cases were in children under 5, and 70% were in children under 15 years of age.³ In the pre-vaccine era, children were exposed early; by 15 years of age, 80% of children were immune to diphtheria from either overt or subclinical infection.⁵ Diphtheria cases are not only limited to young children anymore. This age shift has been attributed to an increased standard of living, smaller families, less overcrowding, and improved hygiene conditions.

There have been reports of re-emergence or persistence of diphtheria from several states of India. According to WHO, in 2016, 2017, 2018 and 2019, the numbers of diphtheria cases in India rose successively to 3,380, 5,293, 8,788 and 9622.⁶ As per data from the Central Bureau of Health Intelligence, India, during 2005-2014, India reported 41,672 cases of diphtheria (average 4,167 per year) with 897 deaths (case fatality ratio 2.2%). As a premier tertiary referral centre of North East, cases have been referred to GMCH from different parts of Assam and from other north eastern states. It has been observed for last few years that number of diphtheria cases attending GMCH is increasing and majority of them are referred from remote places and in very critical conditions at the time of presentation. Considering the above we have taken up this clinicodemographic study on diphtheria cases that have been treated in our Institute.

AIMS AND OBJECTIVES:

- To analyse the demographic distribution of cases and identify the

areas or locality for sensitization and immunization against communicable diseases.

- To evaluate clinical presentation and treatment outcome of diphtheria cases attending a tertiary referral hospital.

MATERIALS AND METHODS:

Data Collection:

The study was conducted at Department of Otorhinolaryngology and Head and Neck surgery, Gauhati Medical College & Hospital (GMCH), Assam from January 2019 to October 2020. The ethical clearance was obtained from the Institutional Ethical Committee to conduct the study and use of hospital data. Data regarding name, age, gender, religion, address, clinical details, complications and treatment outcome have been collected. Information obtained regarding immunization status, whether vaccination is complete, incomplete or none. Children were considered completely immunized if they had received all the recommended doses of diphtheria toxoid for the age including booster as per national immunization schedule. Reasons explained by patient or family members for incomplete or non-vaccination also recorded in the data. All the patients between 0-25 years of age attending Dept of Otorhinolaryngology, GMCH with signs and symptoms of diphtheria were subjected for KLB staining and culture of throat swab on emergency basis. Throat swabs for direct microscopy for KLB and culture for *Corynebacterium diphtheriae* were collected soon after admission. Clinical suspicion and diagnosis was based on presence of febrile illness, throat symptoms, typical pseudomembrane, palatal palsy, lymphadenopathy and oedema in the neck region, airway obstruction, with or without cardiac signs and symptoms. Once diagnosed with diphtheria, case information was given to concerned authority of the hospital for further communication with district health authority. Electrocardiogram (ECG) was done for each patient during the hospital stay to diagnose or rule out any cardiac complications

INCLUSION CRITERIA:

- Patients between the age group 0-25 years admitted with signs and symptoms of diphtheria
- KLB staining positive and culture showing growth of *C. diphtheriae*

EXCLUSION CRITERIA:

- Patients admitted with signs and symptoms of diphtheria but culture shows diphtheriae like bacilli.

Patients were kept in isolation ward for monitoring and management. All the patients with diagnosis of diphtheria were put on parenteral

benzathine penicillin or Erythromycin, depending on penicillin sensitivity and availability. Anti-diphtheric Serum (ADS) was administered to all the patients as single dose between 10000 – 100000 IU depending on severity and extend of disease, as recommended in the Table I. The recommended ADS treatment dosage for paediatric and adult cases were:⁷

Table: I

Diphtheria clinical presentation	DAT dose in IU (# of ampoules)
Pharyngeal or laryngeal disease of 2 days duration	20,000 – 40,000 (2-4)
Nasopharyngeal disease	40,000 – 60,000 (4-6)
Extensive disease of 3 or more days duration, or any patient with diffuse swelling of neck	80,000 – 100,000 (8-10)
Skin lesions only (rare case where treatment is indicated)	20,000 – 40,000 (2-4)

Treatment outcome was defined as either survived or expired. Final data were analysed and compared with relevant available literatures.

RESULTS AND OBSERVATIONS:

During the study period total 24 cases of diphtheria were treated under Department of Otorhinolaryngology, Gauhati Medical College Hospital. Albert stain was positive in all 24 cases & throat swabs also showed growth of *C. diphtheriae* in all 24 cases. There were 17 (70.8%) male cases and 7 (29.16%) female cases with male female ratio 2.4:1. Age distribution of patients were categorized into three groups 0 – 5 years, 5 – 10 years and 10 – 25 years. It was observed that patients between 10 - 25 years of age accounts for 13 cases (54.16%); 5-10 years age group accounts for 10 cases (41.6%) whereas only 1 case (4.16%) was reported between 0-5 years of age group.

In the present study, out of total 24 cases all the patients (100%) presented with febrile illness and throat pain as main presenting symptoms. Typical diphtheric pseudomembrane over tonsil and/or pharyngeal walls was present in all the cases (100%). On the other hand, 20 cases (83.3%) presented with difficulty in swallowing or painful swallowing along with fever and throat pain. 3 cases (12.5%) presented with features of circulatory collapse. Airway obstruction with difficulty in breathing was observed in one case (4.16%). Emergency Tracheostomy was performed in one case (4.16%) to relieve the acute airway obstruction.

Electrocardiogram (ECG) was done for each patient during the hospital stay and there was normal sinus rhythm in 11 cases (45.8%) & sinus bradycardia was seen in 13 cases (54.16%). In our study, 19 cases (79.16%) developed complications of Diphtheria. The main complications noted in descending order were myocarditis - 13 cases (54.16%), followed by cardiogenic shock – 3 cases (12.5%), acute renal failure – 2 (8.3%) and airway compromise – 1 case (4.16%). In the present study, no post diphtheric palatal palsy was noticed.

Out of total 24 cases, only 9 cases (37.5%) has given history of complete vaccination, on the other hand rest 15 cases (62.5%) were incompletely vaccinated or unimmunized. Majority of patient or family members cited migration or shifting of residential location due to erosion of their home land by flood water as the prime cause for missing the routine vaccination schedule. Some of them also had given history of frequent changing of location as migrant labour, may be the reason behind incomplete or missed vaccination.

All the 24 cases were treated with Benzathine Penicillin or Erythromycin depending on sensitivity and availability of the drugs. Anti Diphtheric Serum (ADS) was given to all the cases in appropriate doses according to their severity. In addition to conservative management, 1 patient had undergone tracheostomy operation for acute airway obstruction. 2 patients left the hospital against medical advice without completing their anti-diphtheria treatment and outcome of treatment in these 2 cases are not included in this study. Out of total no. of cases 16 patients (72.7%) recovered & 6 patients (27.3%) succumbed to death.

In this study, majority of patients were from rural areas of Dhubri district accounting for 8 (33.33%) cases followed by Nagaon & Sonitpur district, both account for 4 cases (16.67%) each. 3 cases (12.5%) reported from Kamrup metro and one case each from Kamrup

rural, Goalpara, Kokrajhar, Hojai and Darrang districts of Assam. 17 cases (70.8%) were from lower socioeconomic class & 7 cases (29.16%) from lower middle socioeconomic group of society.

Table: II – Age distribution

AGE	NO. OF PATIENTS	PERCENTAGE
0 – 5 years	1	4.16%
5 – 10 years	10	41.66%
10 – 25 years	13	54.16%

Table: III – Clinical Presentation of the diphtheria cases

CLINICAL PRESENTATION	NO. OF PATIENTS	PERCENTAGE
fever	24	100%
Throat pain	24	100%
Pseudomembrane	24	100%
Difficulty in swallowing	20	83.33%
Circulatory collapse	3	12.5 %
Difficulty in breathing	1	4.16%

Table: IV – Complications among diphtheria cases

COMPLICATIONS	NO. OF PATIENTS	PERCENTAGE
myocarditis	13	54.16%
Cardiogenic shock	3	12.5%
Acute renal failure	2	8.3%
Airway compromise	1	4.16%
Post diphtheric palsy	0	0

DISCUSSION:

The present study was conducted with the aim to analyse the demographic distribution, clinical presentation and treatment outcome of diphtheria cases attending a tertiary referral hospital. Patients between the age group 0-25 years with signs and symptoms of diphtheria with KLB staining positive and culture showing growth of *C. diphtheriae* were only included. Patients admitted with signs and symptoms of diphtheria but culture showing only diphtheriae like bacilli were excluded from this study. That may be one reason for only 24 cases reported during our two years period of study. Meera M. et al (2014) reported 2925 clinical diphtheria cases during her period of study between 2008-2012.⁸ According her study, culture was done for 2905 patients and CD (*Corynebacterium diphtheriae*)/COD (*Corynebacterium* other than diphtheriae) were isolated from throat swab cultures of 550 (18.8%) patients only.⁸ Study conducted by Ray et al (1998) and Patel et al (2004) have also reported low *Corynebacterium* yield (7-12%) emphasizing the relevance of clinical diagnosis and one should not delay immediate and specific treatment of the patient waiting laboratory report.^{9,10} Poor specimen collection on usual throat swab, delayed transportation to the lab, delayed inoculation to the special culture media and prior antibiotic therapy may be some factors for low culture positivity in comparison to clinical diphtheria.¹¹ Pseudomembrane in throat is regarded as hallmark for clinical diagnosis of diphtheria. According to Study conducted by S.N. Singh et al. (2012) typical pseudomembrane in throat was present in 87.1% cases.¹¹

It was observed that majority of our patients (54.16%) were between 10 -25 years of age, whereas 5-10 years age group accounts for 10 (41.6%) cases. Only one case (4.16%) was reported below 5 years of age. Study by Vinayaka H. S. et al (2018) reported 9 (22 %) cases out of total 42 cases were more than 10 years of age.¹³ S.N. Singh et al reported 47.7% diphtheria cases were above 5 years of age, whereas Vinayaka H. S. reported 50 % cases between 5-10 years of age.^{11,13} This changing epidemiology of diphtheria indicates the lack of protective antibodies against diphtheria due to poor coverage with booster doses & declining immunity.¹¹

All the patients (100%) in our study presented with fever and throat pain as main presenting symptoms. On the other hand, 20 cases (83.3%) presented with difficulty in swallowing or painful swallowing in addition to fever and throat pain. Study conducted by Meera M. et al also recorded 100% patients (N = 2925) presented with fever, sore throat, and a pseudomembrane.⁸ Among 34 *Corynebacterium* positive cases studied by S.N Singh et al, fever was present in 33 (97.1%), throat pain and dysphagia in 31 (91.2%), neck swelling in 22 (64.7%), palatal palsy in 6 (17.6%), and membrane was seen in 33 (97.1%) cases.¹¹ Study by Vinayaka H. S. et al found fever (95%) as the main presenting complaint followed in a descending order by, swallowing difficulty (71%), throat pain (71%), bull neck (60%), change in voice (19%), bleeding diathesis (5%) and descending paralysis (5%).¹³

In the present study Electrocardiogram (ECG) was done for each patient during their hospital stay. It is observed that out of total 24 cases, 19 cases (79.16%) developed complications of Diphtheria. The main complications noted in descending order were myocarditis - 13 cases (54.16%), followed by cardiogenic shock - 3 cases (12.5%), acute renal failure - 2 (8.3%) and airway compromise - 1 case (4.16%). No post diphtheric palatal palsy was noticed in any case during our study period. Jayashree et al. have also reported airway obstruction (70.8%) and myocarditis (66.7%) as the most common complications among 48 children admitted in intensive unit.¹⁴ Kadirova R et al. (2000) mentioned myocarditis (22%) as a common complication in their series of study conducted both in children and adult patients.¹⁵ We have reported one case (4.16%) of upper airway obstruction due to diphtheria. Piradov MA et al (2001) demonstrated laryngeal membrane in 76.4% of patients of their study group having airway obstruction.¹⁶ According to them, the other possible mechanism for upper airway obstruction may be soft tissue oedema, extensive pharyngeal disease, bleeding into airway or paralytic closure of larynx.¹⁶ The authors of this study are agreed with Piradov et al for the possible mechanisms explained for airway obstruction in diphtheria cases.

Emergency tracheostomy operation was performed in one patient (4.16%) to relieve acute airway obstruction. In diphtheria patient with upper airway obstruction tracheostomy is always preferable to procure patent airway as intubation may not be successful and can lead to dislodgement of fragile membrane causing further obstruction, bleeding and patient may succumb during procedure as observed by different studies.¹⁴

Table: V -- Comparison of common age group with other studies

Study and Year	Lahari S. et al ¹² 2010	S.N. Singh et al ¹¹ 2012	Alakes kumar et al ¹⁹ 2012	Meera M. et al ⁸ 2014	Basavaraj GV et al ²⁰ 2016	Vinayaka HS et al. ¹³ 2018	Present study
Common age (Years)	15-45	5	5-10	> 20	5 - 10	5- 10	10 - 25
Percentage	69.2	49%	40%	52.6%	74%	50%	54.16

Out of total 24 cases, history of complete vaccination was given by 9 cases (37.5%) and 15 cases (62.5%) were either partially immunized or unimmunized. Migration or shifting of residential location due to erosion of their home land by flood water or shifting to other locality along with the family as migrant labours was the prime cause for missing the routine vaccination schedule for most the partially or unimmunized patients. Analysis of demographic data showed that majority of patients were from Dhubri, Nagaon and Sonitpur districts of Assam and these districts contribute maximum number of migrant labours in Assam and most of them were from low socio-economic status, supporting the migration or frequent changing of residential location as the main reason behind missed vaccination.

Administration of ADS should be started as soon as possible after assessing for hypersensitivity to horse serum; as early administration of ADS is critical for survival.¹⁷ Out of total no. of cases 16 patients (72.7%) recovered & 6 patients (27.3%) succumbed to death and treatment result of two cases could not be recorded due incomplete treatment and follow up. Study conducted by Lahari S. et al (2010) on a diphtheria outbreak in upper Assam, India mentioned 30.8% case fatality out of total 13 cases reported.¹⁸ Whereas, Death reported by S. N. Singh et al (2012), Jayashree et al (2006), and Vinayaka HS et al. (2018) were 48%, 56.3% and 45% respectively.^{11,13,14} In contrast Meera M. et al (2013) reported only 81 deaths (3%) out of total 2925 clinical diphtheria cases reported between 2008 to 2012, diagnosed on clinical signs and symptoms.⁸ Case fatality was 27.3% in our study, almost similar as reported by Lahari et al (30.8%). As a premier institute of Northeast India, comparatively low case fatality in our patients may be attributed to prompt clinical diagnosis of suspected cases, availability and administration of antitoxin, and facilities to manage the complications.

Table: VI --- Comparison of fatality with other studies

Study	Jayashree et al ¹⁴ 2006	Lahari S. et al ¹⁸ 2010	Meera M. et al ⁸ 2014	Singh SN et al ¹¹ 2012	Vinayaka HS et al. ¹³ 2018	Present study
Percentage	56.3	30.8	3 %	48%	45	27.3

Naiditch M J et al (1954) found mortality of diphtheria cases were based on the interval from onset of illness to treatment, with a sharp increase from 4% mortality in those treated with antitoxin within 24-48 hours to 16.1% in those treated on the third day of illness.²¹ Whereas, mortality rates continued to increase with more prolonged intervals, reaching 29.9% in those cases treated 7 or more days after onset.²² Low fatality rate (3%) observed by Meera M. et al, may be attributed to early start of antidiphtheric treatment for all clinical diphtheria cases diagnosed on basis of clinical signs and symptoms only without waiting for laboratory confirmation, whereas we did our study exclusively on KLB and culture positive diphtheria cases only.

CONCLUSION:

Even after tremendous immunization programmes cases of diphtheria are still appearing at some remote areas of the state. Factors contributing to this may be inadequate vaccine coverage, waning vaccine induced immunity in adults, mass population movements, poor living standards etc. Migration or shifting of residential location due to erosion by flood and frequent changing of location as migrant labour are postulated to be as main reason behind incomplete or missed vaccination within our state. As we found that the case fatality rate in cases of diphtheria is still alarming as majority of patients attend hospital lately with complications. Considering the importance of clinical diagnosis of diphtheria and low percentage of culture positivity as observed by different studies, one should not delay specific treatment of diphtheria waiting laboratory report.

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