Original Research Article

Clinical profile and predictors of outcome of patients with diphtheria in tertiary care pediatric centre from Southern India

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ABSTRACT

Background: Diphtheria is still a fatal infectious disease even in this era of universal immunization. The disease has been completely eradicated in most of the developed countries. On the contrary, in developing countries, although the incidence has drastically declined, still account for 80-90% of global burden. The objectives of this study is to study the clinical profile and predictors of outcome of patients with diphtheria.
Methods: All children between the age group of 0 to 15 years admitted with signs and symptoms of diphtheria during January to August 2017 formed the study group. Throat swab for Albert's stain and culture sensitivity were sent in all patients at the time of admission. All children were started on parenteral crystalline penicillin and Anti Diphtheritic Serum as recommended. All details that is demographic data, clinical features, immunization status, complications and outcome were entered in a proforma and analysed. Several variables were compared among the survivors and non-survivors to determine the predictors of outcome. Outcome is defined as either recovered or died.
Results: A total of 42 patients were included in the study group. Among 42 patients, 21 (50 %) were between 5-10 years, 12 (28 %) were between 0-5 years and 9 patients (22 %) were more than 10 years. Most common symptoms were fever followed by throat pain, difficulty in swallowing and bull neck. Alberts stain was positive in 83% of cases and culture positivity in 30% of cases. Myocarditis (47%) was the most common complication followed by acute kidney injury (40%), airway compromise (59%) and thrombocytopenia (42%). A total number of 19 patients died.
Conclusions: Diphtheria is highly fatal disease with increased mortality. Myocarditis was the commonest and most serious complication. Presence of myocarditis, AKI, thrombocytopenia, airway compromise and inadequate immunization are important predictors of outcome.

Keywords: Diphtheria, Myocarditis, Outcomes

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), Karnataka (2011) and Andhra Pradesh (2014) 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) fatal case in an unvaccinated child, to name a few.[4-7]

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]

Objectives

- To study the epidemiology and the predictors of mortality and outcome.
- This would help in early identification of the severity of illness and prioritization of intensive care especially in developing countries with limited resources.

METHODS

We conducted a prospective observational study from January 2018 to August 2018.The study was approved by the committee of ethics on research. Informed consent was obtained from the parents or local guardians of all the participants. All children between the age group of 0 to 15 years admitted with signs and symptoms of diphtheria formed the study group. All patients between the age group of 0 to 15 years admitted with signs and symptoms of diphtheria during January to August 2018 formed the study group. Throat swab for Albert's stain and culture sensitivity was sent in all patients under study at the time of admission. All patients were started on parenteral crystalline penicillin and Anti Diphtheritic Serum (ADS) was given in a single dose as recommended. All patients were evaluated for the presence of complications. All details that is demographic data, clinical features, immunization status, complications and outcome were entered in systematically designed proforma and analysed. Several variables were compared among the survivors and non-survivors to determine the predictors of outcome. Outcome is defined as either recovered or died.

RESULTS

During the study period, a total of 42 patients were admitted in high dependency PICU. Among these 21 patients were male (50%) and 21 patients were female (50%)The Mean age of the patients was (7.44±4.22) with 12 cases being aged 0-5 years accounting for 28%.Children between 5-10 years of age being 21 cases accounting for 50% and 9 cases were above 10 years which constituted about 22% of the group.

Among 42 children that formed the study group, immunisation status was assessed and found that 7 cases (17%) were completely Immunized, 15 cases (36%) were partially immunised and 19 cases (45%) were Un immunized. Immunisation status of 1 case (2%) was not known.

Out of the 42 cases, fever (95%) was 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%) Figure 1.
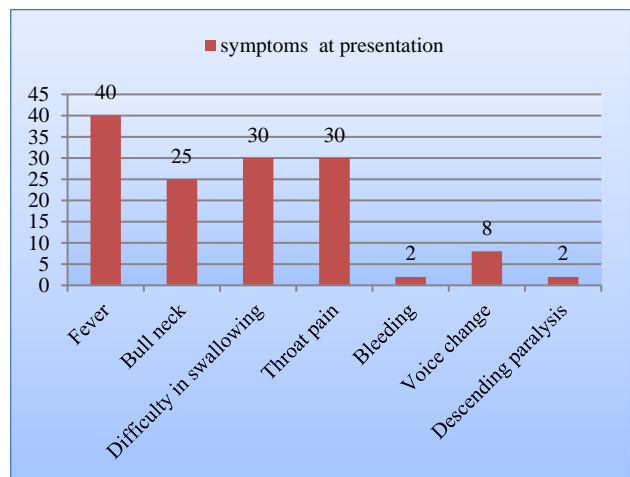

Figure 1: Symptoms at presentation.

Of the 42 patients Alberts stain was positive in 32 cases (76%) and positive throat swab culture was seen in 13 cases (30%) Figure 2.
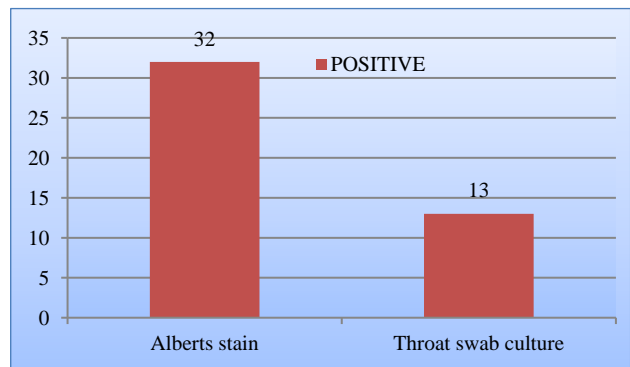

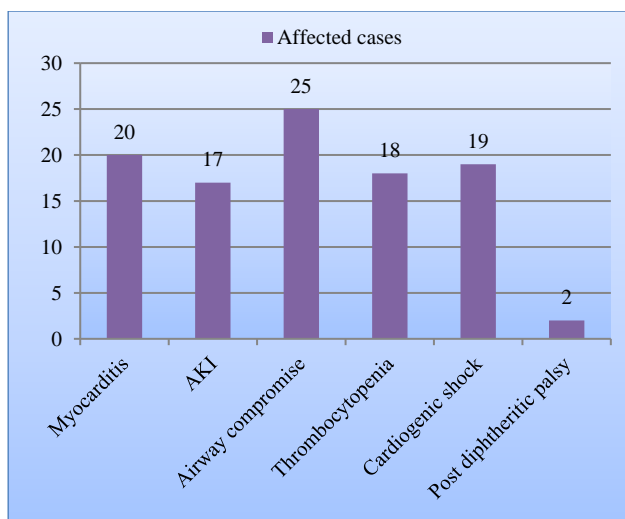**Figure 2: Microbiological results.**

Figure 3: Complications.

The main complications noted in descending order were airway compromise (60%) followed by myocarditis (47%), cardiogenic shock (45%), thrombocytopenia (40%), acute kidney injury (40%) and post diphtheritic palsy (5%) in that order Figure 3.

Table 1: Complications among survivors and non-survivors.

Complications	Non-survivors n=19	Survivors n = 23	P value
Myocarditis	19	1	<0.05
AKI*	13	4	0.0001
Airway compromise	14	11	0.0004
Thrombocytopenia	12	6	0.0001
Cardiogenic shock	18	1	<0.05

AKI: Acute kidney injury

Of the total number of cases 55% recovered and 45% succumbed to the disease with myocarditis being the leading cause of death Table 1.

DISCUSSION

Present study demonstrated that most common age group affected was 5-10 years (21 cases) Data from various other studies also showed similar results. There is an age shift in the occurrence of diphtheria increasingly over 5 years of age. This may be due to several factors like waning immunity with age, lack of booster doses. Among 42 patients, only 17% were completely immunized, 36% were partial and 45% were un immunized. Most of the unimmunized patients are from rural background with poor socioeconomic status. 23 patients (54%) were referred from far off places in a very sick state, in view of non-availability of ADS. Airway compromise (25 patients) was the most common complication observed followed by myocarditis (20 patients), cardiogenic shock

(19 patients), acute kidney injury (17 patients) and thrombocytopenia (18 patients).

Table 2: Comparison of the most common age of presentation with other studies.

Study	Year	Age group	%
Alakes kumar et al[10]	2012	5-10 years	40
Basavaraj GV et al[11]	2016	5-10 years	74
Present study	2017	5-10 years	50

Out of 25 patients with airway compromise, emergency tracheostomy was done in 10 patients and intubation was done in 8 patients. Out of 25 patients, 14 patients succumbed to the illness and 11 patients survived. Myocarditis was observed in 47% (20 patients). Out of 20 patients, 19 patients succumbed and only one patient survived. Myocarditis was mostly observed in second week of illness.[5] Patients received IVIG, with no mortality benefit. Most common ECG abnormality was T wave inversion followed by ST segment depression and heart blocks. Bradyarrythmia was more common than tachyarrhythmia. Acute kidney injury was observed in 17 patients (40.4%).[10] Patients required peritoneal dialysis.[13] patients succumbed to the illness. All 13 patients had myocarditis as well.

Table 3: Comparison of the percentage of mortality with other studies.

Studies	Mortality %
Jayashree et al[12]	56.3
Singh SN et al[13]	48
Present study	45

Out of 42 patients, 19 patients expired accounting for a mortality of 45%. Case fatality rate from various other centres from north India ranged from 32% to 56.3%. Most common cause of death was myocarditis with cardiogenic shock.

CONCLUSION

Diphtheria still remains a potentially fatal disease, primarily due to lack of adequate immunization. There is an age shift in the occurrence of diphtheria increasingly over 5 years of age. Myocarditis, airway compromise, AKI, thrombocytopenia, cardiogenic shock are predictors of poor outcome. Myocarditis was the most important and independent predictor of mortality. Myocarditis with AKI amounts to 100% mortality. There is no role of IVIG in treating diphtheritic myocarditis. But further studies needed. Early administration of ADS can prevent the development of myocarditis. Delay in referral and referral from far off places leads to complications and increased mortality.

Ethical approval: The study was approved by the Institutional Ethics Committee

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