

A study of clinico-etiological profile of Diphtheria with special reference to complications & early outcome.

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Abstract:

Background: Diphtheria is an acute disease caused by exotoxin-producing *Corynebacterium diphtheriae*. Globally, diphtheria has been showing a declining trend due to effective childhood vaccination programs. A substantial proportion of global burden of diphtheria is contributed by India. Diphtheria cases are frequent among school-going children and adolescents. **Objective:** This prospective study was conducted at civil hospital, Ahmedabad, a tertiary care hospital to study incidence, epidemiology and clinical presentation of diphtheria in children up to 12 years in special reference to arising complications associated with early outcome. **Materials and methods :** This retrospective observational study was carried out at civil hospital Ahmedabad in period of 01/09/2019 to 01/02/2020 including all patients admitted in paediatric department under age of 12 years who clinically diagnosed as case as per WHO case definition. **Results:** Out of total enrolled 56 cases, highest incidence found in children between 5 to 10 years of age (39.3%), more in female (53.6%). Unimmunized children (73.2%) were more as compared partially (8.9%) or immunized children (17.9%). Most common complication found was myocarditis (53.6%), followed by palatal palsy (16.1%) and renal failure (7.1%). **Conclusion :** Diphtheria is commonly affecting children between 5 to 10 years of age who are unimmunized which leads to most common complication of myocarditis. Diphtheria can be prevented by proper coverage of vaccines among children.

Key Words: Myocarditis, Unimmunized, Partially immunized.

Introduction:

Diphtheria is a potentially acute disease caused by exotoxin producing *Corynebacterium diphtheriae*, a Gram positive Bacillus. Mortality and Morbidity result from the bacterial toxin that may cause obstructive pseudo membrane in the upper respiratory tract or damage myocardium and other tissues.^{9,1,2} Humans are the only natural reservoir of *C. diphtheria*, although occasionally it has been isolated from variety of domestic animals.^{9,3} Spread occurs in close contact settings through respiratory droplets or direct contact with respiratory secretions or skin lesions.³ The majority of nasopharyngeal

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C. diphtheriae infections result in asymptomatic carriage with clinical disease developing in only about one in seven individuals.^{1,3}

Diphtheria immunization protects against disease but does not prevent carriage. Vaccination with diphtheria toxoid was introduced in 1920s.^{10,9,1} Immunization of children in an era when the majority of older individuals had natural immunity resulted in a dramatic drop in the incidence of diphtheria and an even more rapid decline on the proportion of toxigenic strains isolated, presumably because the selective advantage of the tox gene promotion of greater replication and spread of the organism is lost in an immune host.^{1,2,9} In most western countries, C. diphtheria has virtually been eliminated following effective immunization programs⁹.

However, a resurgence of the disease has been observed in these countries, largely attributed to waning vaccine immunity in adults and importation of cases from the developing world. The situation faced by us in the developing countries is different. Diphtheria still remains endemic with increase in the fulminant complications and mortality in the last two decades, especially in children above 5 years. Factors like inadequate vaccine coverage, poor socio economical standards, overcrowding, delayed reporting to hospital, non-availability and delay in administration of antitoxin further contribute to high mortality. In 2005, India contributed 5826 (71%) of diphtheria cases reported globally. While in 2015 July update from WHO monitoring system data, India still had 6094 cases with total global patients 7382 which makes it 82%.^{10,9,2,11}

So we conducted this study to learn clinical presentation, complication and outcome associated with immunization status of children below 12 years of age.

Aims And Objectives

The study was carried out with following aims and objectives:

- To study of incidence of Diphtheria in children up to 12 years.
- To study epidemiology and clinical presentation of Diphtheria.
- To study complications of Diphtheria.
- To study Correlation between immunization status and severity of Diphtheria and outcome.

Materials And Methods:

- **Study design:** It is a retrospective observational study carried out in pediatric department of civil hospital Ahmedabad, Gujarat, India.
- **Study duration:** 1st of September, 2019 TO 1st of February, 2020

Inclusion criteria

- All patients admitted in pediatric ward up to 12 years of age, who were clinically diagnosed as Diphtheria as per WHO case definition of Diphtheria.

Exclusion Criteria:

- Patients who were >12 years of Age.

All the patients clinically diagnosed as per WHO case definition, were included in study. Detailed histories including age, sex, complaints, immunization history, examination, investigations were noted as per pre-structured Performa. Patients were investigated and monitored during hospitalization and managed as per standard protocols. Investigations: CBC, throat swab for Albert stain, culture and gram stain, RFT done in all patients and CPK-MB, CPK-TOTAL, 2D ECHO, LFT were done as and when required. During hospitalization meticulous history, through clinical examination and required investigations were carried out in all the cases to look for complications and early outcome was noted.

Results:

Table 1: Age wise distribution of patients

Age	N=56 (%)
1-3 YEARS	7(12.5%)
3-5 YEARS	17(30.4%)
5-10 YEARS	22(39.3%)
>10 YEARS	10(17.9%)

Table 2: Sex wise distribution of patients

Sex	N=56 (%)
MALE	26(46.4%)
FEMALE	30(53.6%)

Table 3: Immunization status of patients

Immunization Status	N=56 (%)
Unimmunized	41(73.2%)
Partially immunized	5(8.9%)
Immunized	10(17.9%)

Table 4: Presenting Symptoms And Complications Of Diphtheria:

Presenting Symptoms	N=56 (%)
DYSPHAGIA	53(95%)
THROAT PAIN	51(91.1%)
FEVER	43(76.8%)
RESPIRATORY DIFFICULTY	22(39.3%)
BULL NECK	16(28.6%)
STRIDOR	13(23.2%)
Complications	
MYOCARDITIS	30(53.6%)
RESPIRATORY FAILURE	13(23.2%)
PALATAL PALSY	09(16.1%)

Table 5: Correlation Between Immunization Status And Incidence Of Complications:

Age	Fully Immunized(N=10)		Partially Immunized(N=5)		Unimmunized (N=41)	
	+	-	+	-	+	-
1-3(n=7)	0	1(10%)	0	0	2(0.8%)	4(9.6%)
3-5(n=17)	1(10%)	3(30%)	1(20%)	2(40%)	4(9.6%)	6(2.5%)
5-10(n=22)	2(20%)	2(20%)	1(20%)	0	12(29.3%)	5(12.2%)
>10(n=10)	1(10%)	0	1(20%)	0	7(17.1%)	1(2.4%)
56	4	6	3	2	25	16

+ = with complication, - = without complication.

Table 6: Analysis Between Outcome And Immunization Status.

Immunization Status	Discharged (%) (N=34)	Expired (%) (N=14)	DAMA(%) (N=4)	Total (N=52)
FULLY IMMUNIZED	10(100%)	-	-	10
PARTIALLY IMMUNIZED	5(100%)	-	-	5
UNIMMUNIZED	19(46.3%)	14(34.2%)	4(7.1%)	37
4 unimmunized patients transferred to super speciality.				

In our study, total 56 patients were included with highest number of patients in 5-10 years (39.3%) followed by 3-5 years(30.4%). Female predominance is seen(53.6%), which is statistically not significant. Most of the patients in our study were unimmunized (73.2%). Most patients were from rural area as compared to urban area (62.5%). The most common variety seen is tonsillar Diphtheria (62.5%) followed by tonsillopharyngeal Diphtheria (37.1%). The most common presenting symptom in our study was dysphagia (95%) followed by throat pain (91.1%). Other presenting symptoms were low grade fever (76.8%), Respiratory difficulty (39.3%), Bull neck (28.6%) and stridor (23.2%). The most common found complication in our study is myocarditis (53.6%) followed by respiratory failure (23.2%) and palatal palsy (16.1%). As shown in table 3, immunized patients(n=10) developed complications in 4 cases (40%), while unimmunized patients(n=41) developed complications in 25 cases (61%). But the difference is statistically not significant(p=0.48).

As it suggests among unimmunized patients incidence of complications increased from i.e. 0.8% in 1 to 3 years to 29.3% in 5 to 10 years, which is statistically significant (p=0.01).

In our study, Patients who were fully and partially immunized were successfully discharged(100%) , where as in unimmunized patients higher mortality rate seen(34.2%) which is statistically significant (p value=0.02).

Discussion:

In present study we enrolled total 56 patients ,seen that occurrence of disease was more common in females(53.6%) as compared to males (46.4%), same observation was seen in MESHARAM RM et al which is statistically insignificant and observed as an incidental finding. In present study and MESHARAM et al most of the patients were from rural area

which might be due to lack of awareness about immunization, shortage of resources, illiteracy. The median age of diphtheria cases in most of the published studies was <5 years.¹² In our study most of the patients were from 3-5 and 5-10 years of age group which was (30.4%) and (39.3%) respectively. In 1-3 years of age group incidence was 12.5%, this could be because of strong coverage of primary immunization. In previous year studies higher incidence in preschool children was due to lack of awareness about primary immunization but due to more and more awareness programs about immunizations rate of primary immunization is increasing but coverage of booster dosages needs more strengthening. The coverage of primary diphtheria vaccine in the country is around 80%, whereas the coverage of diphtheria boosters, although not available, is expected to be low. Due to unsatisfactory immunization coverage with DPT vaccine a greater number of cases was reported. Out of total 56 cases 73.2% of cases were totally unimmunized, and 8.9% of cases were partially immunized. In HIRAL et al percentage of unimmunized patients who got the disease was higher. In present study it was observed that children who were fully immunized and developed diphtheria had better outcome and chances of complications were low as compared to children who were unimmunized($p=0.02$). This may be only because disease in who were previously immunized was milder and less fatal and so that better outcome was seen.

The most common presentation was dysphagia seen in about 95% of the patients. Some of the patients were presented with fever (76.8%) and throat pain (91.1%). Dysphagia as a presenting symptom was seen only in 28(59.6%) patients in MESHRAM RM et al. which might be due to delayed consultation at hospital by patients in our study. In MESHRAM RM et al (100%) patients were presented with fever and 95.7% were presented with throat pain.

The systemic complications were Myocarditis (53.6%), respiratory failure (23.2%), and palatal palsy (16.1%). Systemic side effects are most commonly occurs due to absorption of toxin from local site of infection. The most common complication seen in MESHRAM et al is also Myocarditis (53.6%). Myocarditis require meticulous hospital management and monitoring, because cases were diagnosed in second week of illness as local disease improves. The early and prompt treatment prevents mortality. Specific antitoxin is mainstay of management to neutralize circulating toxin. Total four patients were referred to cardiac super speciality for worsening of myocarditis and all were unimmunized.

The outcome in our study is found better in fully and partially immunized(100% discharged in both) as compared to unimmunized patients(34.2% mortality) which is statistically highly significant($p=0.02$).

Conclusion:

Diphtheria is one of the most commonly seen vaccine preventable disease. Immunization is one of the gold standard methods to prevent incidence and serious complications of the diseases. Diphtheria toxoid should be given to infants as a primary series of three doses, followed by three appropriately spaced booster doses to ensue long term protection.

Higher Incidence of Diphtheria and related complications was seen in children who were totally unimmunized and chances of complication seen increased with advancing age.

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