Original Research Article

# Study of cardiac complications in Diptheria cases in southern region of Maharashtra

Garud B[1*], Chavan S[2], Agarkhedkar R[3], Salunkhe S[4], Gaiwale S D[5]

{[1]Assistant Professor [2]Professor, [3]Professor & HOD, Department of Paediatrics} {[4]Associate Professor [5]Associate Professor, Forensic Medicine And Toxicology} Dr. D.Y. Patil Medical College, Hospital And Research Centre, Pimpri, Pune, Dr. D.Y. Patil Vidyapeeth, Pune, Maharashtra 411018, INDIA.

**Email:** balkrishna860@gmail.com

## Abstract

**Background:** Diphtheria is still a fatal disease even in the era of universal immunization. Diphtheria myocarditis, one of the serious complications of respiratory diphtheria may cause death if not recognized and treated properly. **Aims and Objectives:** The present study carried out with aim to find out prevalence of Cardiac Complications in diphtheria Patients in paediatric practice. **Materials and Methods:** The present study was carried out on total 36 children reported to tertiary care southern Maharashtra setup with specific signs and symptoms. Study was entirely based on clinical criteria for diagnosis of diphtheria such as cough, fever, difficulty in swallowing and membrane in throat. Evaluation done on duration of present signs and symptoms, history of any contact, immunisation, past similar history, more stress was given on immunisation. For confirmation of the diagnosis done by microbiological throat swab culture and sensitivity on samples of collected patients. **Results**: The most common symptoms were fever seen in 33 cases, pain in throat in 24 cases, difficulty in swallowing in 22 cases, cough in 13 cases, difficulty in breathing in 2 cases, and nasal regurgitation in 1 case. Most common complication observed was myocarditis seen in 4 patients and majority of patients. The ECG's were taken in all cases suspected to have myocarditis. Out of that (4) cases showed, ECG changes s/o myocarditis. Prolonged QTc was the commonest change noticed.ST-T changes seen in 1 Patient. A total five patients died. **Conclusions:** Myocarditis was commonest and serious complication of respiratory diphtheria. Increase in vaccination coverage and improvement of socioeconomic status are all effective preventive measures to reduce the incidence of diphtheria.

**Keywords:** Cardiac involvement, Diphtheria, Immunization, culture, Sensitivity.

[*]**Address for Correspondence:**
Dr Garud B, Assistant Professor, Department of Paediatrics, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune, Dr. D.Y. Patil Vidyapeeth, Pune, Maharashtra 411018, INDIA.
**Email:** balkrishna860@gmail.com

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## INTRODUCTION

Infection or infectious process is the interaction of a pathogenic micro-organism and a macro-organism under the influence of environment. If, as a result, the equilibrium of the organism's interaction with environment is disturbed, an infectious disease ensues. A necessary condition is that the micro-organism must be an "Extreme Irritant" overcoming "Physiological action against the disease (Povlov) and disturbing its normal functioning.[1] "Disease and pathological processes follow same laws of evolution as man and the higher animals" (Mechanikov).Definition: "Diphtheria is an acute infectious and communicable disease characterized by involvement of respiratory system, the local production of membrane and general symptoms caused by absorption of toxin"[2] "Toxin production is a very characteristic property of diphtheria bacillus and although strains exist which are a virulent and produce no toxin, all strains from the acute sore throat produce toxin to some degree".- R. Tanner Hawlett.[3] Diptheria was recognized at least 2 thousand years ago when it was prevalent in the middle east and was known as the "Egyptian or Syriac ulcer".[1] In Greek; Diphthera – meaning – a membrane.[1]Causative agent *corynebacterium diphtheria* are irregularly staining gram

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+ve, nonmotile, nonsporulating, pleomorphic bacilli. The club shaped appearance of bacillus results from attempting to grow the bacillus on media that are nutritionally inadequate (Loefler's media). On Tellurite media, three colony types can be distinguished:- Mitis, Gravis, intermedius. Mitis colonies are smooth, black and convex, they do not ferment starch and glycogen and are haemolytic.[4] Intermedius strains are more likely to produce haemorrhagic lesions.[5]Predominant strains are gravis followed by mitis and intermedius forms[(6)]. "The organism has adopted itself towards existence in a highly immunized population, so that a carrier of it may be entirely symptomless or may merely complain of a mild sore throat".[5]The availability of specific antitoxin, anti-diphtheritic serum since 1890, has reduced the morbidity and mortality from the disease.[7]

## METHOD AND MATERIAL

This is prospective clinical study of cardiac complications of diphtheria in paediatric patient in tertiary care centre.

### Study population:

Patients admitted in paediatric ward up to 18 years of Age, enrolled after fulfilling inclusion criteria with due consent of their parent. Selection of patient entirely based on clinical basis

### Inclusion criteria:

I. Clinical criteria for diagnosis of diphtheria:
   a. h/o pain in throat, cough, fever difficulty in swallowing and breathing.
   b. Presence of membrane in throat or anywhere else.

II. Clinical criteria for diagnosis of post diphtheritic paralysis:
   a. H/o diphtheria in the recent past or at the time of occurrence of paralysis.
   b. Past history of sore throat, pain in throat, ever with or without Bull Neck.
   c. Paralysis of accommodation, pharyngeal paralysis.
   d. S/o myocarditis.

### Methodology

Approval from the Institutional Ethical Committee was obtained before commencing the study. Written and Informed Consent was obtained from all patients. The patients were informed regarding the purpose, procedures, risks and benefits of the study in their own vernacular language. A standard proforma for study participants were used for collection of data. Routine investigations such as complete hemogram, protein, throat swab culture sensitivity, urine routine and microscopy, chest X-ray were carried out. Case identification was based on the following criteria: (i) Clinical: based on the review of information in the patient's charts, (ii) Laboratory: based on results of throat swab cultures, Supportive evidence: derived from diagnostic tests and results of X-rays. HAIs was suspected based on the CDC criteria.

## OBSERVATIONS AND RESULTS

In this study total 36 Confirmed cases of Diphtheria in the paediatric age group were studied, of which 5 cases died, 1 case had palatal palsy and 4 patients developed myocarditis.

**Table 1:** Age wise distribution of the Diphtheria cases

| Age (years) | No. of Cases | Percentages (%) |
|---|---|---|
| 1 – 5 | 12 | 33% |
| 6 – 10 | 15 | 41.6% |
| 11 – 15 | 9 | 25 |
| **Total** | **36** | **100%** |

**Table 2 : Gender wise distribution of the Diphtheria cases.**

| Age in years | Gender of the case | | Percentages (%) |
|---|---|---|---|
| | Boys | Girls | |
| 1 – 5 | 8 (22.2%) | 4 (11.11%) | 33% |
| 6 – 10 | 5 (13.8%) | 10 (27.7%) | 41.6% |
| 11 – 15 | 5 (13.8%) | 4 (11.11%) | 25% |
| **Total** | **18** | **18** | **100%** |

(chi square test = 3.11, df = 1, p>0.05)

Among the 36 cases;15 cases (41.6%) were of the age group of 6-10 yrs. of which females were more contributing to 10 cases (27.7%).

**Table 3:** Analysis of presenting complaint (Symptoms)

| Symptoms | No. of Cases | Percentages (%) |
|---|---|---|
| Fever | 33 | 91.1% |
| Pain in throat | 24 | 66.66% |
| Difficulty in swallowing | 22 | 61.1% |
| Cough | 13 | 36.11% |
| Swelling of Neck | 7 | 19.4% |
| Difficulty in breathing | 2 | 5.5% |
| Change in voice | 2 | 5.5% |
| Bleeding through nose | 2 | 5.5% |
| Nasal regurgitation | 1 | 2.7% |

Fever was the commonest presenting symptom contributing in 91.1% of cases

**Table 4:** Table showing age wise contribution of mortality in diphtheria cases

| Age (yrs.) | Total No. of cases | No. of death | Percentage (%) of deaths in corresponding group |
|---|---|---|---|
| 1 - 5 | 12 | 3 | 25% |
| 6 - 10 | 15 | 2 | 13.3% |
| 11 – 15 | 09 | -- | -- |
| **Total** | **36** | **5** | **13.8%** |

Maximum number of deaths occurred in 1-5 years age group (25%) followed by 6-10 years age group (13.3%).

**Table 5:** Distribution of cases according to Gender and Gender-specific case fatality

| Gender | No. of cases | Percentage (%) | No. of deaths | Percentage (%) of deaths in corresponding group |
|---|---|---|---|---|
| **Boys** | 18 | 50% | 2 | 5.5% |
| **Girls** | 18 | 50% | 3 | 16.6% |
| **Total** | **36** | **100%** | **5** | **22.10%** |

(Z= 0.16, p>0.05)

There is no statistically significant difference between no. of cases in male and female. Although mortality rates were higher in female patients.

**Table 6:** Rural – Urban incidence with relative mortality in each group

| Area | No. of cases | Percentage (%) | No. of deaths | Percentage (%) of deaths in corresponding group |
|---|---|---|---|---|
| **Rural** | 28 | 77% | 4 | 14.2% |
| **Urban** | 8 | 23% | 1 | 12.5% |
| **Total** | 36 | 100% | 5 | 13.8% |

(Z= 0.55, p>0.05, Z= 0.014, p>0.05)

Statistically there is no significant difference between incidence as well as deaths in Urban and Rural cases of diphtheria. (Z= 0.014, p>0.05)

**Total 7:** Correlation between Immunization status and of Diphtheria cases incidence and proportionate mortality

| Status of immunization | Boys (%) | Girls(%) | Total (%) |
|---|---|---|---|
| **Fully immunized** | 4 (11%) | 0 (0%) | 4 (11.11%) |
| **Partially immunized** | 4 (11%) | 5 (13.8%) | 9 (25%) |
| **Unimmunized** | 10 (25%) | 13 (36.11%) | 23 (63.88%) |
| **Total** | 18 | 18 | 36 (100%) |

(X2= 6.45, df= 1, p<0.01)

Statistically there is significant association found between immunization status and incidence of diphtheria cases. Out of the 36 cases, only 4 (11%) cases were immunized, 63.88% were unimmunized. That shows importance of immunization on the incidence and prognosis of diphtheria.

**Table 8:** Correlation between immunization status and morbidity

| Morbidity | No. of cases | Partially immunized | Unimmunized | Immunized |
|---|---|---|---|---|
| **Myocarditis** | 4 | 1 | 3 | 0 |
| **Post Diphtheria Paralysis** | 1 | 0 | 1 | 0 |
| **DIC** | 4 | 0 | 4 | 0 |

All the patients who had developed complications were unimmunized except one who developed myocarditis and was partially immunized.

**Total 9:** Anatomical type of diphtherial patch and mortality

| Anatomical types | No. Of Cases | Percentage (%) | No. of death | Mortality rate |
|---|---|---|---|---|
| **Uni-tonsillar** | 10 | 27.7 | 0 | 0 |
| **Bi-tonsillar** | 15 | 41.5 | 2 | 13.3 |
| **Uvular** | 1 | 2.7 | 0 | 0 |
| **Extensive** | 9 | 25 | 3 | 33.3 |
| **No patch** | 1 | 2.7 | 0 | 0 |

Extensive: Tonsillar + Posterior pharyngeal + Uvular + Palatal. The incidence of involvement of both tonsils by diphtherial patch was maximum i.e. 41.5%. Out of the total 5 deaths, that occurred during the study, 3 had extensive Diphtheria, contributing 33.3% to total mortality. Followed by bi-tonsillar diphtherial patch having 13.3% mortality.

**Table 10:** Occurrence of myocarditis in diphtheria and its relation with mortality

| No. of cases with myocarditis | Percentage (%) | No. of deaths of myocarditis | Proportionate mortality to corresponding group |
|---|---|---|---|
| 4 | 11.11% | 2 | 50% |

11% of the cases in this study showed evidence of myocarditis. Patients with myocardial involvement contributed 50% of the deaths that occurred in the study population.

**Table 11:** Correlation between anatomical type of diphtherial patch and the occurrence of myocarditis

| Anatomical types | No. of cases | No. of cases with myocarditis | Percentage (%) of death in corresponding group |
|---|---|---|---|
| **Uni-tonsillar** | 10 | 1 | 10% |
| **Bi-tonsillar** | 15 | 1 | 6.6% |
| **Uvular** | 1 | 0 | 0.0% |
| **Extensive** | 9 | 2 | 22.22% |

This table clearly shows the increased incidence of diphtheritic myocarditis in the patients who had extensive involvement of diphtherial patch. Out of 4 cases of diphtherial myocarditis, 2 (50%) cases had anatomically extensive involvement contributing maximum 22.22% of deaths out of remaining 50% cases each had unilateral and bilateral tonsillar involvement.

**Table 12:** ECG abnormalities in diphtheria myocarditis

| ECG Changes | No. of cases | Percentage (%) |
|---|---|---|
| **ST- T change** | 1 | 25% |
| **Prolonged QTc** | 3 | 75% |

ECG's were taken in all cases suspected to have myocarditis. All cases (4), showed. ECG changes s/o myocarditis. Prolonged QTc was the commonest change noticed.

## DISCUSSION

In our prospective study, the peak incidence was found in the age group of 6 to 10 years contributing 41.6% of the total cases followed by 1 to 5 years age group contributing 33.3% of the total cases. This agrees with findings of K. Basappa (1962,46) who showed 25% and 24% contribution by above groups in his study. Similar observation was found by S.R. Sengupta, A.G. Joshi in their study in Aurangabad20 which showed 50% contribution by 2-5 yrs. age group. Theodore *et al.*. (1962) reported the highest incidence in 5 to 9 years age group. This and studies by other western workers indicate an age shift in incidence of diphtheria from preschool to early school age. This disparity can be explained on the basis of extensive immunization during infancy protecting, the preschool children, where as waning immunity in older children making them more susceptible to diphtheria.19 Most of the studies agree on a peak incidence in the age group of 1 to 5 years. Bhargava *et al.*. (22,53,54,55) have found a maximum incidence in the age group of 2 to 5 years which is correlated well in our study. It is well known that the age of child has an important bearing in determining the mortality from diphtheria, being more fatal in the early years of life. Generally, in infants, symptoms of cold and cough are ignored, and it is only when the child begins to get difficulty in respiration, refuses to take feeds or develops swelling of neck that he is brought to the paediatrician. It is also probable that some cases pass undetected in the early part of illness due to incomplete examination and lack of high index of suspicion on the part of medical attendant.

### Sex wise distribution of cases:

In our prospective study equal number of cases of Boys as well as girls were equal. This observation correlates with study by Basappa (1963,46) which found almost equal incidence of cases among males and females.Some authors

Suri and Khosla 1964, Chandra *et al.*. (197118) reported higher predilection of female sex. Thus, there is no unanimous opinion in this regard. But a significant difference in the occurrence of disease in males and females in different age groups is established by most of the studies. Basappa (1960,46) described a sex ratio of M:F 1:1.3. Brooks *et al.*. 31 in United States also reported a slightly higher attack rate for males in the birth to 4 years age group, but it was higher for females in all other age groups. Immunization rates were also more in female i.e. 36.11% as compared to male i.e. 25%. Which is well correlated with Patel VV, Patel BH *et al*... Indian Journal of community medicine April (2013,53)

**Rural-Urban Incidence:**

Diphtheria is found to have higher incidence in rural than Urban community. In this study also, out of 36 patients, 77% belonged to rural community and 23% belonged to urban community. Thus, a higher incidence is noted in the rural population. This higher incidence among rural cases in this study are primarily referred from Karnataka and Maharashtra border area, this high endemicity represents situation in border area this may be due to less immunization coverage in rural area as compared to the urban area.

**Incidence in immunized Vs unimmunized children:**

Brooks *et al.*. (1974. 31) has quoted the incidence based on national immunization survey in 1967 and 1968, in United States. The attack rate for unimmunized children was 70 times higher than the rate for children with three or more injections. The rate for children who had received 1 or 2 doses of toxoid was six times the rate or those who had received 3 or more doses. In the study carried by Guha Mazumdar *et al.*. (1968,45) only 3.1% patients were immunized cases, however, the course of the disease was mild. Dutta and Ayyagiri 45 found 3.01% children out of total patients were stated to have received 3 doses of DPT and yet they fell victim of disease. In our study, out of 36 cases, 4 cases were fully immunized contributing (11%), 9 patients (25%) were partially immunized. All these cases developed diphtheria 2 to 5 years after the last dose. Thus, the incidence 63.88% among unimmunized children was 6 times that in completely immunized cases. These observations go in conformity with the findings of various workers. Immunisation significantly alters the clinical severity of diphtheria. Brooks *et al.*. (1974,31) described that the entire spectrum of clinical severity in immunized patients was significantly shifted towards mild disease. In his study, only 1.5% (3 patients) of 203 who had 3 or more injections of toxoids died. In contrast, 12.8% (167 patients) of the 1300 unimmunised patients expired. This difference is highly significant (P0.0005). Mazumdar's 1968 study in Calcutta 45 found that whenever diphtheria occurred in immunized children (3.1% of total cases), the disease was mild in nature in all of them and no fatality took place.

All the cases who had developed myocarditis and diphtheritic neurological complication were unimmunized. Except one case of myocarditis who is the partially immunized. The partially immunized cases included those who had missed the second or third DPT doses of primary immunization.

**Clinical Presentation And Duration of illness at the time of presentation**:

Bhargava and Bhatta 196022 showed that when specific treatment is carried out on the first day of disease, death rate is 0.3% on the 3rd day 4% on 4th day 12% and on subsequent days 25%. Also the classic textbook description11 states "If specific treatment is provided on the first day of disease, mortality may be reduced to less than 1%, delay in treatment until 4th day may be associated with a 20 fold increase in mortality". The present study shows the majority of patients (59.19%) presenting with history of illness dating 1 to 4 days. The case fatality was more among the patients who had presented within 1 to 4 days of illness. Specific antitoxin was administered to all the patients on admission itself, the increase in duration of illness directly represents the delay in administration of antitoxin. Almost all studies on diphtheria have described the progressive rise in mortality with delay in ADS administration.

**Analysis of presenting symptoms:**

Fever was the commonest symptom in this study 91.1% cases presented with it. Other common complaints at presentation were difficulty or pain in swallowing, pain in throat 66.66%, difficulty in swallowing 61.1%. In our study well correlated with Bhargava *et al.*.22 have described the common presenting symptoms as fever 89% cough 62%, pain in throat 36%, difficulty in breathing33%. The frequency of bullneck and stridor in the present study was 19.4% and 5%. Thus the bullneck indicate an ominous prognostic sign in diphtheria patients. The poor prognosis suggested by Bullneck and stridor were highlighted in the studies of Bhargava (1960.22) and Shrivastava (1968.19)

**Analysis of Cardiac Complications in Diptheria patients**

11% of the cases in this study showed evidence of myocarditis. Patients with myocardial involvement contributed 50% of the deaths that occurred in the study population. The increased incidence of diphtheritic myocarditis in the patients who had extensive involvement of diphtherial patch. Out of 4 cases of diphtherial myocarditis, 2 (50%) cases had anatomically extensive involvement contributing maximum 22.22% of deaths out of remaining 50% cases each had unilateral and bilateral tonsillar involvement. ECG's were taken in all cases suspected to have myocarditis. All cases (4), showed. ECG changes s/o myocarditis. Prolonged QTc was the

commonest change noticed. The Sunil Samdani *et al.*. 2017 study shows, the ECG changes were sinus tachycardia (68.3%), T wave inversion (20%), ST segment depression (13.3%), right bundle branch block (5%), multiple atrial ectopics (3.3%). The case fatality rate in our study was 25% (15 patients). Present study Shows similar result as ECG's were taken in all cases suspected to have myocarditis. All cases (4), showed ECG changes s/o myocarditis. Prolonged QTc was the commonest change noticed. And ST-T change seen in 1 case.

## CONCLUSION

Cardiac involvement is a common complication of infection with C. diphtheria and is associated with high mortality. As diphtheria can be prevented by adequate vaccination, efforts should be maximized for high vaccine coverage with booster doses.

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