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RESEARCH ARTICLE

A STUDY OF DIPHTHERIA CASES WITH SPECIAL REFERENCE TO NEUROPATHY

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ADS- Anti diphtheritic serum,
DP-Diphtheritic polyneuropathy,
GBS-Guillain-Barre Syndrome,
NCV-Nerve conduction study.

ABSTRACT

Background: Diphtheria is an acute infection caused by Corynebacterium Diphtheria spreads by human contact. During 2007-2011, a total of 55 countries worldwide, reported >20,000 cases of Diphtheria and among them India reported the most cases (n=17,926).**Objective:** To study the frequency, clinical profile, progress and the outcome of neuropathy amongst Diphtheria cases. **Methodology:** A retrospective study of 26 patients who developed weakness following acute Diphtheria was done. **Result:** The incidence of Diphtheritic neuropathy in survived cases of diphtheria in our study was 29.8% (N-26/87). Maximum numbers of Children with neuropathy in this study were in the age group of 5-10 years (16/26) with median age of presentation being 7 years. The incidence is more in Male in our study (19/26). 25 out of 26 patients were partial/ unimmunized. All 26 children had features of bulbar palsy. Amongst them, 14 children had features of isolated palatal palsy. One child had unilateral lower motor neuron facial palsy and one had 6th cranial nerve involvement & Quadruparesis was seen in 4. Among these 26 patients, majority (19/26) of patients had received ADS during their hospital stay. **Conclusion:** Diphtheria is a vaccine preventable disease so, Routine vaccine administration, prompt diagnosis, early treatment, early administration of ADS and early recognition of complications and treatment of such will reduce associated morbidity and mortality.

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INTRODUCTION

Diphtheria is an acute infection caused by *Corynebacterium Diphtheria* spreads by human contact. During 2007-2011, a total of 55 countries worldwide, reported >20,000 casesof Diphtheria and among them India reported the most cases(n=17,926) (WHO). Its pathogenicity is due to the production of 62kD polypeptide exotoxin- that inhibits protein synthesis and causes local tissue necrosis with special affinity for myocardium, adrenals and nerve endings. Paralysis of the palate and hypo-pharynx is an early local effect of toxin (Hadfield, 2000). Involvement of myocardium and peripheral nerves occurs later in course of illness so the pathophysiology in some cases is suspected to be immunologically mediated. The features of diphtheritic neuropathy include nasal quality of voice, difficulty in swallowing and nasal regurgitation. Cranial neuropathies occurs late - usually in 5th week, leading to occulo-motor and ciliary paralysis, which can cause strabismus, blurred vision or difficulty in accommodation. Symmetrical polyneuropathy occurs late from 10th day to 3 months after the pharyngeal infection and causes principally motor deficits in distal muscles of extremities with proximal progression is more commonly observed. Complete neurological recovery is likely (Mohanta KD-1974 and Nelson Textbook). We present a retrospective study of 138 patients of Diphtheria from tertiary care center from May 2017 to December 2017.

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Objective

To study the frequency, clinical profile, progress and the outcome of neuropathy amongst Diphtheria cases.

MATERIALS AND METHODS

A retrospective study of 26 patients who developed weakness following acute Diphtheria was done. The patients with other evident cause for weakness like GBS, electrolyte disturbance etc. were excluded. The records were reviewed and information regarding demographic profile, immunization status, clinical presentation, treatment received (medical & or surgical including ventilator care) & the outcome were recorded in proforma. C. Diphtheriae was isolated in throat swab culture in 14 and Albert stain was positive in 4 out of 138 cases. NCV study was performed in 4 cases who presented with limb weakness & gait disturbance. All these patients were treated with crystalline penicillin for 10 days & anti diphtheria

serum was given to 96 patients as per the availability. Complications were treated as per standard guidelines. Total 37 patients were tracheotomised and kept on mechanical ventilator for variable time as per the progress. 38 children died following serious complications.

OBSERVATION

The maximum numbers of children were in the age group of 5 to 10 years (65.2%). This could be due to increased exposure in these school age children &also due to weaning of immunity with increasing age to primary dose. Male children were greater in number than female (M: F is 1.87:1). This could be because the male children were given more preference to seek medical care during illness by the caretaker. It may also be due to males are genetically more vulnerable to various infections than female.

Table 1. Age-sex distribution

Age	Male	Female	Total
<5	26	11	37 (26.8%)
5-10	55	35	90 (65.2%)
>10	9	2	11 (7.9%)
Total	90 (65.2%)	48 (34.7%)	138

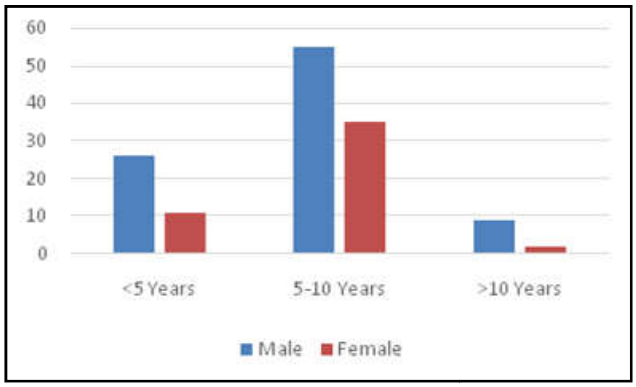

Fig. 1. Age-Sex Distribution

Table 2. Vaccine Status

	Completely immunized	Partially immunized or Unimmunized
Male	18	72
Female	7	41
Total(N-138)	25 (18.1%)	113(81.9%)

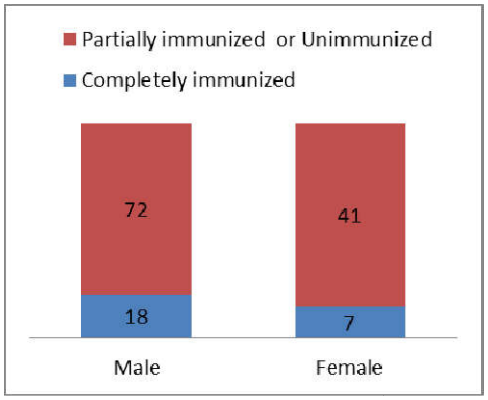

Fig. 2. Vaccine Status

Only 18.1% of children were completely vaccinated for their age. There was no difference in the vaccine status between two sexes. (P= 0.43). The national coverage of complete DPT vaccine is 78%.Poor educational background & the myths about vaccination might be responsible for low immunization coverage amongst this class of children.

Table 3. Treatment Modalities

Treatment Modality	
Crystalline penicillin	138
Anti-diphtheria serum	96
Tracheostomy & ventilator care	37
IV immunoglobulin G	01

Table 4. Outcome

TOTAL	138
Discharged	87
Expired	38
DAMA	8
Transfer to cardiology department	3
Transfer to nephrology department	2

87 children who dischargedwere followed up to 3 months for weakness. Total 26 children developed weakness (29.8%).

Table 5. Age wise distribution of weakness (n = 87)

Age	Total no	With weakness
<5 years	20	07 (8.04%)
5-10 years	62	16 (18.3%)
>10 years	05	03 (3.4%)
Total	87	26 (29.88%)

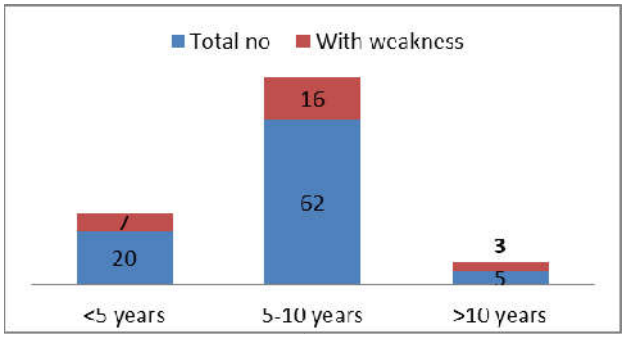

Fig. 3. Age wise distribution

Maximum no cases were in the age group of 5- 10 years (18.3%) with mean age of 7 years. This may be due to highest number of diphtheria cases were also in the same age group in present study. The mean duration of onset of weakness was 18 days from the onset of first symptoms.In children > 10 years of age, weakness was observed in 3 out of 5. The total numbers of children in the said age group were very less so no significant conclusion can be mad.

Table 6. Sex -wise distribution of weakness (n=87)

	Total no	With weakness
Male	61	19 (21.8%)
Female	26	7 (8.04%)

Overall male children who developed weakness were more than female (19 vs. 07) but statistically there was no significant difference observed amongst two sexes. (p = 0.77 by Chi-square test).

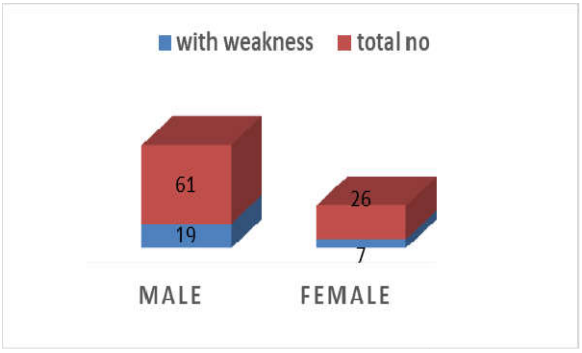

Fig. 4. Sex wise distribution

Table 7. Correlation between immunization status and weakness (n=87)

	Total no	No of patients with weakness
Partial/unimmunized	71	25 (28.73%)
Fully immunized	16	01 (1.14%)
Total	87	26(29.88%)

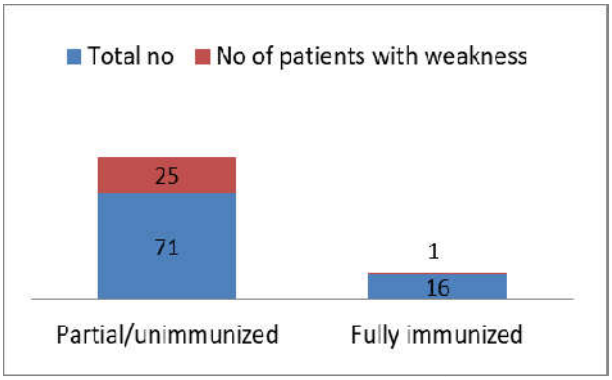

Fig. 5. Correlation between immunization status and weakness

Out of 26, majority (25) children were either unvaccinated or only partially vaccinated for their age. Similarly only one child out of 16 who were completely vaccinated developed weakness. Apparently it showed remarkable benefit of vaccine to reduce the risk of weakness but the observed difference is not statistically significant as the p value by Fisher exact test is 0.11. (Table7).

Table 8: Correlation between ADS& weakness (n-87)

ADS	No. of patients	Weakness	%
Given	55	19	21.8%
Not Given	32	07	8.04%
Total	87	26	29.84%

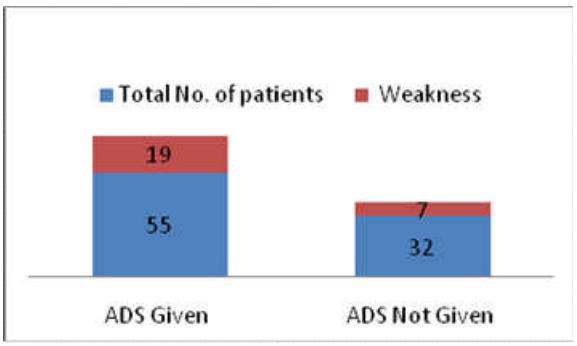

Fig. 6. Correlation between ADS& weakness

Out of 87, 21.8% of children with weakness had received ADS whereas 8.04% had not been given ADS. Overall 19 children from ADS group & 7 from non-ADS group developed weakness. There was no statistical significance between the two groups as the p value = 0.2.This suggests no remarkable benefit from ADS in preventing the neuropathy however it requires large study size to derive conclusion.

Table 9. Presenting clinical features (n=87)

Clinical feature	
Bulbar palsy	26 (29.8%)
Cranial nerve palsy	2 (2.2%)
Quadruparesis	4 (4.5%)

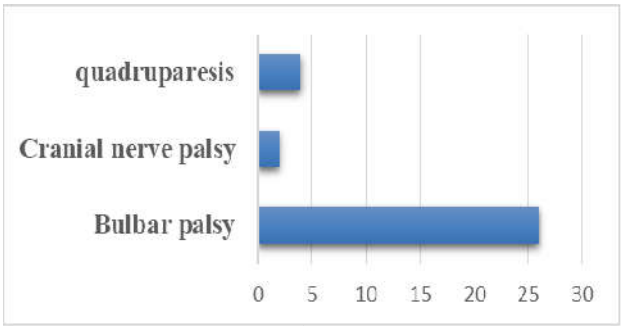

Fig. 7. Presenting features

Bulbar palsy was the most common neurological deficit including isolated palatal palsy in 16.09% (14/87).VIth&VIIth cranial nerve palsy was seen in one child each. Quadruparesis was seen in 4. There was no case of respiratory paralysis.

Table 10. 3 Months Follow Up (N=26)

	Fully Recovered	Partially Recovered	No Follow-Up
Bulbar Palsy (26)	8	9	9
Quadruparesis (4)	-	2	2
Cranial Nerve palsy(2)	-	1	1

Table 11. Features of diphtheritic polyneuropathy in various studies

	OUR STUDY N= 26	Dr D Manikyamba et al[6] (2013) N= 13	AFP SURVELLIAN[(1)]CE(2002-2008) N=15	KANWAL SK et al[(5)] N=48
AGE Group(Years)	2-12(mean age=7yr)	5-13	<15	4.25(median age)
IMMUNIZATION STATUS				
Complete	03.84%	-	-	-
Partial	15.38%	47%	-	-
Unimmunized	80.78%	53%	-	100%
LATENCY IN DAYS	12-42 (mean duration =18 days)	15-30	-	15
ISOLATED PALATAL PALSY	53.84%	60%	15%	6%
LIMB INVOLVEMENT	15.38%	40%	85%	94%
RECOVERY IN DAYS	16-90days	21-102 days	-	-

9 children lost to follow up. Out of remaining 17 children who were followed up, 8 recovered completely & 9 had residual weakness.

Summary & Conclusion

1. Amongst all cases of Diphtheria, 65.2% of children were between 5 to 10 years of age group. Gradual weaning of immunity against the diphtheria toxin with increasing age & increase exposure risk at school may explain this.
2. Male: Female ratio was 1.87: 1. More preference to male child for seeking the medical care during illness & relatively decreased infection risk amongst the genetically less susceptible females may explain the observed difference.
3. Only 18.1% of children were completely vaccinated with age appropriate dosage of DPT. There was no significant difference in the vaccine coverage between two sexes. Low literacy level & the myths towards the vaccine could explain the poor vaccination.
4. All the cases were treated with appropriate antibiotics for optimal duration & ADS was given to 96 out of 138. 37 children required tracheostomy & post procedure ventilator support for variable duration.
5. 87 children recovered & discharged to home. 36.9% of children died following acute complication.
6. 29.8% of children out of survived (87) developed neuropathy following acute infection.
7. Maximum cases (16/26) of neuropathy were in the age group of 5-10 years with mean age of 7 years. Mean duration of onset of neuropathy was 18 days. Overall male children with weakness were more in number.
8. Majority of children who developed weakness were either unvaccinated or only partially vaccinated for DPT vaccine. Study revealed remarkable benefit of vaccine but statistical significance could not be proved.
9. In our study we found no significant benefit of ADS to prevent weakness.
10. Bulbar palsy was the most common neurological deficit present in all (29.8%). Isolated palatal palsy was present in 14 (16.09%). Quadruparesis was developed in 4 (4.59%).
11. 9 children lost to follow up. Out of17 who were followed, 8 recovered completely & 9 had residual weakness.

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