

# CLINICAL FEATURES OF DIPHTHERIA IN THAI CHILDREN: A HISTORIC PERSPECTIVE

Chitsanu Pancharoen<sup>1</sup>, Jutarat Mekmullica<sup>2</sup>, Usa Thisyakorn<sup>1</sup>  
and Suchitra Nimmannitya<sup>3</sup>

<sup>1</sup>Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand;

<sup>2</sup>Department of Pediatrics, Bhumibol Adulyadej Hospital, Bangkok, Thailand;

<sup>3</sup>Queen Sirikit National Institute of Child Health, Bangkok, Thailand

**Abstract.** To study the clinical and laboratory features of childhood diphtheria, the cases of 381 children with clinical and bacteriological diagnoses of diphtheria who were treated at the Children's Hospital between 1976 and 1985 were reviewed. Of these, 191 were males and 190 were females. The mean age was 4.6 years. Approximately 75% of the patients had no history of immunization. Common manifestations of diphtheria included patch (100%), fever (92.4%), upper respiratory tract infection (91.6%), upper airway obstruction (42.3%), hoarseness (36.7%), and bull neck (11.3%). The mean duration of fever prior to admission was 3.3 days with a range of 0-11 days. Patch sites included the tonsils (91.9%), the pharynx (55.9%), the larynx (27.8%) and others (24.4%). Complications included upper airway obstruction (42.3%), cardiac complications (10.0%) and neurological complications (4.7%). The mortality rate was 5.8%. There were significant associations between death and the presence of bull neck, laryngeal patch, airway obstruction and cardiac complications. Early recognition and prompt treatment will decrease complications and mortality in this group of patients.

## INTRODUCTION

Diphtheria caused by *Corynebacterium diphtheriae*, used to be a major life-threatening illness in many countries. The disease usually occurs as membranous nasopharyngitis or obstructive laryngotracheitis and may cause serious complications resulting in significant mortality (American Academy of Pediatrics, 2000). In Thailand, the number of reported cases of diphtheria has been declining during the past decades (Division of Epidemiology, 1990-1998). However, recently reported numbers of diphtheria cases have shown an upward trend (Pancharoen, 2001) and a few small outbreaks of the disease have been reported each year (Pitaksiripan *et al*, 2000; Saipan *et al*, 2000). Re-emergence of the disease is

possible in the near future. Moreover, the mortality rate among patients with diphtheria has increased, probably due to the non-recognition of the disease and the consequent delay in diagnosis and treatment (Viriyautsahakul *et al*, 1994). We conducted this study in order to review the natural history of diphtheria in children in Thailand.

## PATIENTS AND METHODS

Prospectively recorded data of children aged 0-15 years with the diagnosis of diphtheria, who were treated in the Children's Hospital (now the Queen Sirikit National Institute of Child Health) from 1976-1985, were reviewed. The diagnosis of diphtheria was based on clinical presentation and bacteriological confirmation. Only those with a positive culture for *Corynebacterium diphtheriae* were included in this study. The data collected included age, sex, clinical presentation, site of patch, complications, laboratory findings, and mortality. Descriptive data were analysed using mean, standard deviation, range and percent-

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Correspondence: Dr Chitsanu Pancharoen, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University Hospital, Rama IV Road, Bangkok 10330, Thailand.

Tel/Fax: 66 (0) 2252-8181-9 ext 3349, 66 (0) 2256-4930

E-mail: chitsanu.p@chula.ac.th

age. The risk factors for fatal illness and their association with patient age ( $\leq 1$  year) were tested by Pearson's chi-squared test and logistic regression, as were the associations between age ( $\leq 1$  year) and bull neck, laryngeal patch, and other complications. The level of significance was defined as a p-value  $< 0.05$ .

## RESULTS

Of the 381 children who met the criteria for recruitment, 191 were males and 190 were females. The mean age of the study patients was  $4.6 \pm 2.7$  years with a range of 0.4-13.4 years. The mean body weight was  $14.2 \pm 5.6$  kg. The history of previous immunization against diphtheria was considered: 74.7% of patients had not received diphtheria toxoid; 8.2% had an uncertain history.

Common manifestations (and their incidence) included: patch (100%), fever (92.4%) upper respiratory tract infection (91.6%), difficulty breathing (42.3%), hoarseness (36.7%) and bull neck (11.3%). The mean duration of fever prior to admission was  $3.3 \pm 2.1$  days with a range of 0-11 days and a peak at 3 days. Patches were located on the tonsils (91.9%), in the pharynx (55.9%), in the larynx (24.8%), and in various other sites, *ie* uvula, nostril, epiglottis (27.8%). Unilateral tonsillar patches were found in 51 of 351 cases (14.5%); 29 were right-sided and 22 were left-sided. There were

seven cases (1.8%) of isolated laryngeal diphtheria, four of which needed emergency tracheostomy. Isolated nasal diphtheria was found in 3 patients (0.8%). There were no cases of skin or vaginal diphtheria in this study.

Complications included: upper airway obstruction (42.3%), cardiac complications (10.0%), neurological complications (4.7%). Tracheostomy was performed in 82 cases (21.5%). The cardiac complications found were myocarditis, cardiac dysrhythmia, heart block and nonspecific electrocardiographic changes of, mostly, the ST segment or T-wave. The neurological complications included cranial nerve (CN) paralysis (mostly involving CN IX and X), limb paralysis and cerebral anoxia secondary to severe airway obstruction. There were associations of patient age ( $\leq 1$  year) with both airway obstruction and neurological complications (Table 1).

Complete blood counts showed a mean hematocrit level of 34.8%, a mean white blood cell (wbc) count of 16,280 cells/mm<sup>3</sup> and a mean differential count of neutrophils of 66.8%. Urinalyses showed proteinuria in 52.7% of cases (trace = 18.6%; 1+ to 4+ = 34.1%) and pyuria in 2.7% of cases (wbc  $> 10$ /high power field). Throat swab cultures revealed co-infection with *Streptococcus pyogenes* in 25/282 cases (8.9%). The mean level of serum aspartate transaminase (AST) was 66.7 IU/l with a range of 20-661 IU/l; an AST level  $> 100$  IU/l was found in 20/169 cases (11.8%).

Table 1  
Association and odds ratio between variables of study patients.

Variables	Variables	p-value	Odds ratio	95% CI
Death	Bull neck	$< 0.001$	19.91	7.72 - 51.39
	Laryngeal patch	0.004	3.38	1.42 - 8.09
	Upper airway obstruction	0.003	3.94	1.50 - 10.30
	Cardiac complication	$< 0.001$	27.92	10.30 - 75.68
	Neurological complication	1.0	0.96	0.12 - 7.55
	Age $\leq 1$ year	1.0	1.30	0.17 - 10.00
Age $\leq 1$ year	Upper airway obstruction	0.037	2.52	1.03 - 6.17
	Cardiac complication	1.0	0.89	0.20 - 3.98
	Neurological complication	0.011	5.48	1.64 - 18.33

Note: CI = Confidence interval.

The mortality rate was 5.8%. The causes of death were severe airway obstruction, cardiac complications and pulmonary complications. There were significant associations between death and the presence of bull neck, laryngeal patches, airway obstruction and cardiac complications (Table 1).

## DISCUSSION

Our study shows that the majority of children with diphtheria presented with fever and pharyngotonsillar patches. Some had dyspnea and hoarseness when the patches extended to the larynx. Although rarely, it is possible to find no pharyngotonsillar patches in diphtheria patients with airway obstruction. The characteristics and extension of patches assist in differentiating diphtheria from infectious mononucleosis (Pancharoen *et al*, 2000). Moreover, our previous study showed that almost all Thai children had been infected by Epstein-Barr virus by the age of six (Pancharoen, *et al*, 2001).

The patients with upper airway obstruction, the most common complication, almost always presented with dyspnea and/or hoarseness and sometimes needed tracheostomy. Delayed complications, *ie* those affecting the cardiovascular neurological systems, usually appeared after the first week of illness and were common and occasionally severe. Airway obstruction and cardiac complications were important causes of death among our patients.

The treatment of diphtheria includes penicillin and diphtheria antitoxin; corticosteroids have been shown not to prevent myocarditis or neuritis (Thisyakorn *et al*, 1984).

In order to prevent disease, primary injections of diphtheria toxoid (as DTP, DTaP or DT) should be given to all children of 2, 4, 6 and 18 months of age and again at 4-6 years of age. At the age of 10-12 years, dT should be given to boost immunity against diphtheria and tetanus. Waning immunity may be seen in 15% of adolescents and young adults (Tantawichien *et al*, 2000). In the future, dT may be used to replace tetanus toxoid (TT)

to maintain general population immunity against diphtheria and tetanus.

Diphtheria remains a serious, life-threatening disease with a high fatality rate. It is possible that diphtheria may re-emerge in Thailand in the future, especially among older children and young adults. Early recognition and prompt treatment will reduce complications and mortality.

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