

Low incidence of children with acute epiglottitis after introduction of vaccination

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ABSTRACT

INTRODUCTION: The aim of this retrospective case series is to describe the epidemiology, symptoms and findings of acute epiglottitis in hospitalized patients after the introduction of the *Haemophilus influenzae* type B (HIB) vaccine and to identify any symptoms or findings predictive of a prolonged hospital stay.

MATERIAL AND METHODS: Medical records on all patients discharged with the International Classification of Diseases 10 diagnostic code DJ051, acute epiglottitis, from January 1997 to December 2012 were reviewed. A total of 41 patients were identified.

RESULTS: In all, 37 patients were included, only one of whom was a child. The dominating symptom was a sore throat (97.2%). A hoarse voice was found in 20 patients (58.8%), and 14 patients (40.0%) were drooling. Thirteen patients (36.1%) had trouble breathing. Nine patients (24.3%) were diagnosed with abscess. Two adults tested positive for HIB. The average length of hospitalization was 6.1 days. The average stay in the intensive care unit was 1.2 days for patients who were not intubated and 4.0 days for patients who were intubated or tracheotomised. Six patients (16.2%) were intubated. One patient (2.7%) was directly tracheotomised.

CONCLUSION: Our study shows that the incidence of adult acute epiglottitis seems to remain unchanged compared with a previous investigation from the same geographical region. The disease is potentially life-threatening, and intubation or tracheostomy was required in 18.9% patients in this study. Respiratory distress had the largest impact on the length of hospitalization.

FUNDING: not relevant.

TRIAL REGISTRATION: not relevant.

Acute epiglottitis (AE) is a potentially lethal disease in both children and adults [1]. After the introduction of the *Haemophilus influenzae* type B (HIB) vaccination in Denmark in 1993, the total number of patients diagnosed with AE has declined. This is owed to the fact that AE primarily occurs among infants and children. Two years after the introduction of the vaccination programme, a 72% reduction of the number of children suffering from AE has been observed [2]. This decline has been observed in many of the western countries [3-6]. However, a similar decline in AE has not been seen in

adults among whom the incidence remains in the 1-4/100,000/year range [1, 5, 7, 8]. Accordingly, a Danish study from Roskilde found an incidence of 1.9/100,000/year in the 1996-2005 period, which is comparable to a national incidence of 2.1 [9]. In their similar Danish study from South-West Denmark (1987), Tveterås & Kristensen estimated an incidence of adult acute epiglottitis of 0.88/100,000/years [1]. Furthermore, this study showed that 19 out of 43 cases were cases of adult epiglottitis in the ten-year period preceding the introduction of the HIB vaccination [1].

After the introduction of the HIB vaccination in Iceland and Finland, retrospective studies have shown that the bacterial aetiology is dominated by streptococci types [6]. In Finland, which was the first Scandinavian country to introduce the HIB vaccination in 1986, a study from 2011 showed only one case of AE was caused by HIB among 308 adult cases [4].

The aim of this study is to describe the epidemiology, aetiology, symptoms and findings of AE in hospitalized patients after the introduction of the HIB vaccine in a regional hospital in Denmark and to identify symptoms or findings predictive of a prolonged hospital stay.

MATERIAL AND METHODS

Population

A total of 41 patients were discharged from the Oto-rhino-laryngological Department of The Hospital of South-West Jutland with the diagnosis acute epiglottitis (International Classification of Diseases (ICD)-10 diagnostic code DJ051) in the period from January 1997 to December 2012. The Hospital of South-West Jutland covers a geographical area counting 225,000 inhabitants. AE was defined as an inflammation of the supraglottic structures, including the epiglottis, the false vocal cords, the epiglottic folds and lingual tonsil areas.

All patients, regardless of age, with the diagnosis DJ051 were included. Patients found not to fulfill the definition of AE when reviewing their medical journals were excluded.

The medical files were retrospectively reviewed independently by two of the authors, and three patients were subsequently excluded. One patient was excluded due to a missing medical file.

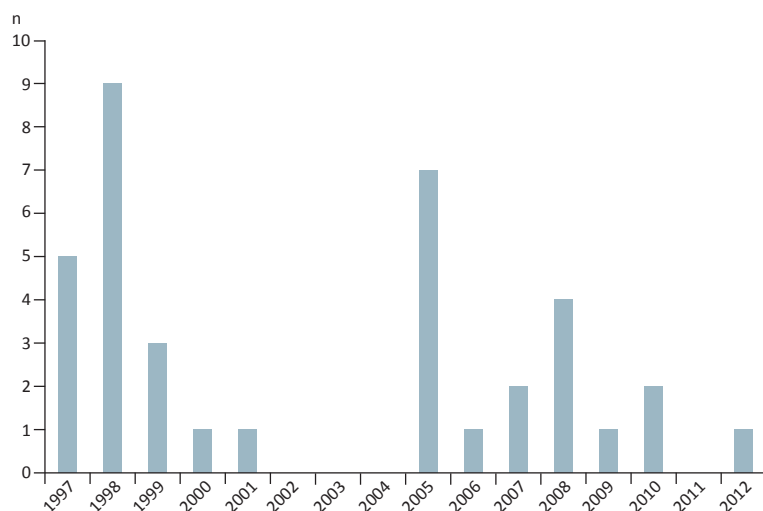
ORIGINAL ARTICLE

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Dan Med J
2014;61(4):A4788

FIGURE 1

Number of patients diagnosed with acute epiglottitis in 1997-2012.



Collection of data

Data were registered on age, gender, symptoms, clinical and paraclinical findings at admission, co-morbidity, smoking, admission to intensive care unit (ICU), intubation, medical treatment and number of days admitted.

Permission from the Danish Data Protection Agency was obtained before the retrospective review of medical journals.

The data analysis was carried out with STATA version 10, College Station, Texas, USA. Data are presented as descriptive frequency tables in the case of categorical variables. For continuous variables, data are presented by averages and 95% confidence intervals for normally distributed data.

Admission time, used as an outcome variable, was analysed with multiple linear regression where clinical findings and treatment were included as explanatory variables in the analyses.

Trial registration: not relevant.

RESULTS

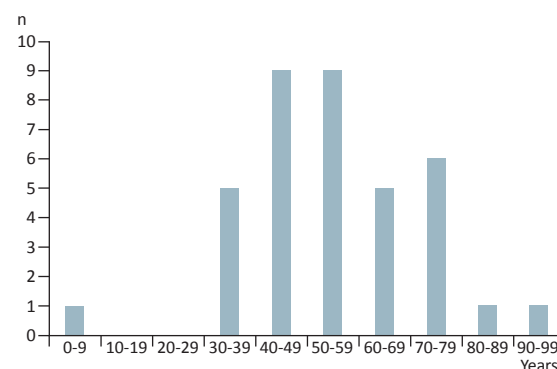
Epidemiology

Figure 1 shows the distribution of AE cases per year. During the 16-year period, four years were without any AE incidence. The highest number of cases observed was nine in 1998, which is equivalent to an incidence of 4.0/100,000/year. The average incidence for the whole period was 1.0/100,000/year. **Figure 1** also shows that 46.0% of the patients were admitted within the three-year period from 1997-1999.

Figure 2 shows the number of AE cases in relation

FIGURE 2

Patients diagnosed with acute epiglottitis in 1997-2012 by age group.



to age. The patients were between seven and 93 years of age, the average age being 54 (95% confidence interval (CI) 48.3-59.8). There was only one child (a seven-year-old). In all, 28 (75.7%) were males and nine (24.3%) were females, which is equivalent to a male-to-female ratio of 3.2:1.

The seasonal variations are presented in **Figure 3**. A total of 13 (35.1%) were diagnosed during winter (December, January and February) and 12 (32.4%) during spring (March, April and May). Additionally, six patients were diagnosed during the summer (June, July and August) and six during autumn (September, October and November).

Symptoms and signs

Table 1 illustrates that the dominating symptom on arrival to hospital was a sore throat (97.2%). A hoarse voice was found in 20 patients (58.8%), and 14 patients (40.0%) had trouble swallowing their own saliva. Six (16.7%) patients presented with stridor. Out of the eight patients with breathing difficulties on admission, three were at risk of respiratory arrest. The most frequent objective finding was oedema of the epiglottis, which was seen in 35 (94.6%) patients. A more modest swelling of the epiglottis was found in 11 (29.7%) patients, and eight patients (21.6%) had fibrin coatings or ulcerations of the epiglottis. Four (10.8%) patients were diagnosed with an abscess in the epiglottis at the time of admission and an additional five (13.5%) patients were diagnosed with an abscess during the hospital stay. One patient (2.7%) was suspected of an abscess, and one patient (2.7%) had an abscess on the right false vocal cord.

The average length of hospitalization was 6.1 days (95% CI 5.00-7.10). A total of 26 (70.3%) patients were admitted to the ICU for observation. Six (16.2%) patients were intubated, and subsequently one was tracheotomised. One (2.7%) patient was directly tracheotomised

without intubation within the first day of hospitalization. The average time of stay at the ICU was 1.2 days for patients who were not intubated and 4.0 days for patients who were intubated or tracheotomised.

Table 1 also shows the average length of hospitalization for patients with different symptoms and findings. The p value is compared to the patients who did not receive the treatment given or did not present with the current symptoms or findings. The factors associated with a longer hospital stay, were respiratory distress ($p = 0.001$), stridor ($p = 0.01$) and intubation ($p = 0.02$).

Three patients were readmitted, including one patient who was readmitted the day after being discharged because of subjective complaints. However, the patient was not found to have respiratory difficulties and readmission was limited to one day.

The other two patients were readmitted 12 and 25 days after being discharged, respectively. Before discharge, direct laryngoscopy had shown nearly normal conditions in the endolarynx. Re-hospitalization lasted 14 and seven days, respectively.

Microbiology

Throat swabs were performed in nine (37.8%) patients, and nine patients had blood cultures taken. In 11 patients there was a positive finding of bacteria growth. HIB was found in two patients, a 40-year-old and a 47-year-old. Both had positive throat swabs and one also had a positive blood culture. In addition, both haemolytic and non-haemolytic streptococci were detected in four patients. One patient was infected with *Staphylococcus aureus*, one patient with *Fusobacterium gonidiaformans* and one with anaerobic Gram-negative rods. Eight patients (47%) had negative swab results, and ten (71.4%) had negative blood cultures. Blood culture results could not be obtained in two patients.

Treatment

A total of 34 (91.9%) patients received intravenous antibiotics during their hospital stay. The most commonly used therapeutic modalities were combination therapy with cefuroxime $1.5 \text{ g} \times 3$ and metronidazole $500 \text{ mg} \times 3$ (26.5%) or monotherapy with ampicillin $1 \text{ g} \times 4$ (26.5%). The three patients who received no intravenous antibiotics were all treated with oral antibiotics. In all, 23 out of these 34 patients were later treated with oral antibiotics. The average duration of treatment with intravenous antibiotics before switching to oral antibiotics was 4.4 days. Data on the duration of treatment were only available for 21 patients. Seventeen patients (45.9%) were treated with corticosteroids.

DISCUSSION

This study has identified 37 cases of AE over a 16-year-

period. Only one of the 37 cases was a child. The incidence of AE in this study was shown to be 1.0/100,000/year, which is similar to a previously reported incidence of adult AE in the same geographical region of Denmark in the period 1975-1984 [1]. This study shows that cases of childhood AE have almost disappeared: only one case in a 16-year-period was identified compared with 24 cases of AE identified among children during the 1975-1984 period in the same geographical population.

This study and other previous studies demonstrate that the epidemiology of AE has changed since the introduction of the HIB vaccine [4, 6]. Only one of the patients was a child, and although the vaccination programme in Denmark does not have 100% coverage [9], the effect of herd immunity can protect the rest. This corresponds well with other studies [5, 7]. The estimated incidence in adults was 1.0/100,000/year, which is comparable to the 0.77/100,000/year seen in Iceland and to the 1.9/100,000/year reported from the Roskilde study [6, 9].

This study shows that the most significant predictors of length of hospitalization were breathing difficulties, stridor and intubation. Treatment with antibiotics and steroids did not significantly shorten the hospitalization period.

Additionally, a trend towards seasonal variation in the occurrence of AE was observed with more cases being admitted during the winter period (December, January and February). Seasonal variation was previously reported, with some studies showing the highest number of AE admissions in the summer, and in other studies during the winter period when upper respiratory infections are more frequent [4, 6, 10]. This article



FIGURE 3

Seasonal incidence of acute epiglottitis in 1997-2012.

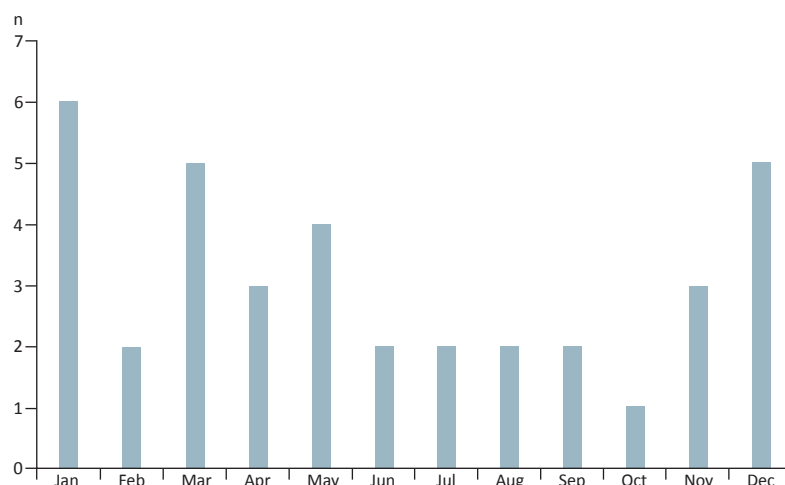


TABLE 1

Length of hospitalization related to symptoms and signs. The parameter of age, gender and smoking were used as confounders.

	Patients		Average length of hospitalization, days	p-value
	n	%		
Symptoms				
Sore throat	35	97.2	6.37	0.45
Hoarseness of voice	20	58.8	7.69	0.64
Drooling	14	40.0	7.43	0.22
Breathing diffuculties	8	22.2	9.63	0.007
Signs				
Oedema of the epiglottis	35	94.6	7.01	0.41
Redness of the epiglottis	33	91.7	6.51	0.33
Modestly swelling of the epiglottis	11	29.7	7.14	0.42
Fibrin layer on epiglottis	8	21.6	6.98	0.60
Epiglottic abscess	6	16.2	6.51	0.33

shows a male-to-female ratio of 3.2:1, which is consistent with previous studies that have reported male-to-female ratios ranging from 1.2:1 to 4:1 [8, 11].

Patients in this study presented with symptoms and findings in the form of sore throat, affected voice and pain on swallowing. This is in line with what previous studies have found [4, 6, 7, 9, 12].

Only two out of the 37 patients were identified with AE with a HIB infection. Furthermore, in a minority of cases, it was possible to identify the type of bacteria causing the infection. The aetiology of bacterial AE in an adult population can be associated with a variety of bacteria types. This study found *Staphylococcus aureus*, *Fusobacterium gonidiaformans* and anaerobic Gram-negative rods as well as HIB. This may lead to speculations that the aetiology of AE in adult differs much from that seen in children. It was previously suggested that the aetiology of AE among adults may include a variety of different microorganisms including viruses and fungi [1, 4, 6].

Other Scandinavian studies have shown a similarly low number of adult patients with AE caused by HIB [4, 6]. Mayo-Smith et al showed a link between HIB bacteraemia and compromised airways [5]. In accordance with previous studies in vaccinated populations, streptococcal and staphylococcal infections dominated [4, 13].

In many of the identified cases with AE in adults, infection of other than supraglottic structures was also seen. This can lead to speculations that the initial origin of the infection may be neighbouring structures or the spread of an initial epiglottic infection to other structures.

The recommended antibiotics in the treatment of AE are second- and third-generation cephalosporins or

ampicillin. Fluoroquinolones are recommended for patients with penicillin allergy [8, 13]. In this study, the most frequently used antibiotic treatment was a combination of cefuroxime 1.5 g \times 3 and metronidazole 500 mg \times 3 or monotherapy with ampicillin 1 g \times 4.

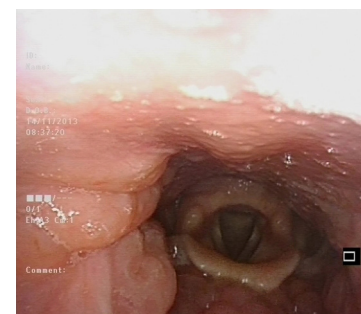
Cefuroxime may be combined with metronidazole with a view to targeting anaerobic bacteria. Treatment with intravenous antibiotics in this study was consistent with the recommendations from previous studies [8, 12].

Patients presenting with drool, stridor and respiratory distress should be monitored in the ICU as these patients often follow a more severe clinical course [5]. Children have been found to have a higher risk of intubation, since the space of the endolarynx in children is smaller than in adults. Moreover, they have a more reactive lymphoid tissue in the supraglottic region. Seven patients required respiratory assistance with intubation (six) or tracheotomy (one). The only child in this study was intubated. All seven patients displayed the before-mentioned symptoms. All patients were intubated in the ICU or surgical ward within the first 24 hours. The 19 non-intubated patients who were admitted to the ICU stayed there for an average of 1.5 days. In our study, this period of time seems to be sufficient to avoid the need for intubation at an oto-rhino-laryngological ward.

Three patients were readmitted. This would have been difficult to anticipate as both symptoms and findings were almost normal at discharge. No patients died in our study.

CONCLUSION

Our study shows that the incidence of adult AE seems to remain unchanged compared with a previous study covering the same geographical region, which correlates with the aetiology being different in adults than in children. However, it is remarkable that only one child was identified with AE in the study period in comparison with 24 children identified in the 1975-1984 study covering the same area in Denmark [1]. This may be owed to HIB vaccination. The disease is potentially life-threatening, and intubation or tracheostomy was required in approximately one in five patients in this study.



Direct laryngoscopy showing normal epiglottis, vocal folds and arytenoids.

It is recommended that patients who have difficulty in swallowing, stridor, respiratory distress and sudden onset of symptoms should be transferred to the ICU for close observation. If the subjective and objective conditions improve the first day, it is recommended that the patient is assessed to determine whether the ICU stay needs to be continued.

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ACCEPTED: 17 December 2013

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk.

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