

Epidemiology of *Haemophilus influenzae* type b meningitis in Taiwan, 1997 and 2000

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In order to determine the incidence of *Haemophilus influenzae* type b (Hib) meningitis in Taiwan, we analyzed the National Health Insurance Research Database (NHIRD). We identified cases that were younger than 5 years old and diagnosed with Hib meningitis from the NHIRD in both 1997 and 2000. Sixteen and 8 children with Hib meningitis were identified in the NHIRD for 1997 and 2000, respectively. The majority of cases were 2 years old and under. The overall fatality rate was 8.33%. Assuming similar proportions of Hib meningitis in cases of meningitis with identified causes and meningitis without identified causes, the annual incidence of Hib meningitis in children younger than 5 years old was estimated to be 5.57 and 3.22 per 100,000 in years 1997 and 2000, respectively. The incidence of Hib meningitis in Taiwan is lower than in western countries and other Asian countries. This is consistent with the notion that Hib meningitis incidence is low in Chinese populations. The decline in incidence from 1997 to 2000 is likely a result of the introduction of a self-paid Hib vaccine in Taiwan, starting in 1993. The availability of the NHIRD provides an extra tool for the epidemiological study of infectious diseases in Taiwan and can be valuable for similar studies.

Key words: Epidemiology, *Haemophilus influenzae*, incidence, meningitis

Haemophilus influenzae type b (Hib) is one of the leading causes of bacterial meningitis in many countries [1-4]. Aside from meningitis, Hib also leads to many invasive diseases such as pneumonia, epiglottitis, septic arthritis, and sepsis [5]. Hib disease is now preventable. Its incidence has been markedly reduced in North America and Europe as a result of systemic immunization of all children [6,7]. Invasive Hib infection was believed to be uncommon in Asia. However, recent studies found that in some areas of Asia the incidences were similar to those of western countries [4,8].

There have not been any previous population-based data to describe the incidence of Hib meningitis in Taiwan. Wang and Lin reported on a hospital-based study indicating that Hib was the leading cause of and accounted for 41% of bacterial meningitis in children less than 5 years old in Taiwan from 1992 to 1994 [9]. A prospective surveillance based on active reports of hospitals from 1996 to 1997 in Taiwan showed that the

annual incidence of invasive Hib disease was 1.6 per 100,000 in children less than 5 years of age [10]. Most of the available results were based on hospital surveys. It would be preferable to produce Hib meningitis incidence in Taiwan based on population study.

Since the coverage of National Health Insurance (NHI) in Taiwan's population is above 96%, its database may be considered a reliable epidemiological source. The National Health Insurance Research Database (NHIRD) contains comprehensive records of medical care of NHI members. In this study, we analyzed the NHIRD as a substitute for population-based surveillance.

Materials and Methods

The NHIRD is a comprehensive outpatient and inpatient care record of the Bureau of National Health Insurance (BNHI). We analyzed 2 databases in NHIRD, which were inpatient database and medical center database. The inpatient database is a 'sub' database, which contains one-twentieth of all inpatient medical care records of every hospital in Taiwan using systematic sampling. The systematic sampling was performed

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each month and then combined to become the annual database. In addition, a medical center database, which is a subset of the NHIRD and contains all outpatient and inpatient medical care records for 9 medical centers, has been available for academic research since 1999.

For this study, we analyzed records from the inpatient database and the medical center database to estimate the incidence of Hib meningitis in Taiwan. All inpatient records in patients less than 5 years old with a primary or secondary diagnosis of bacterial meningitis (International Classification of Diseases [ICD]-9 code 320) were identified from both the inpatient database and the medical center database in 1997. The inpatient records with a diagnosis of Hib meningitis (ICD-9 code 3200), meningitis with other known etiologies, and meningitis with unknown etiologies could only be identified from the medical center database.

The case numbers identified from the inpatient database are the total case numbers that had been admitted to a hospital due to bacterial meningitis in that year. We estimated the proportion of Hib meningitis among the known etiologies cases using the data from the medical center database. We assume that the proportion of Hib meningitis is the same between the inpatient database and the medical center database. Thus, the overall Hib meningitis case numbers in the NHIRD may be estimated. Furthermore, we analyzed the inpatient records in patients less than 5 years old with a primary or secondary diagnosis of bacterial meningitis in the medical center database in 2000 for comparison. The annual incidence rate was calculated according to the national population younger than 5 years old in 1997 and 2000, which was obtained from the website of the Ministry of Interior Statistical Information Service.

Results

In 1997, a total of 132 admissions of bacterial meningitis (ICD-9 code 320) were identified from the medical centers subset. Eighty three had defined etiological bacteria (Table 1). Among the cases of known etiologies, Hib represented 19.28% of cases (16/83) of known pathogens. There were 23 cases of bacterial meningitis in the inpatient database, so that total bacterial meningitis cases were 460 in 1997. Therefore, the estimated case-load of Hib meningitis was 89. The annual incidence of Hib meningitis cases under 5 years old was calculated to be 5.57 per 100,000 (89/1,599,094) in 1997.

In 2000, 203 admissions of bacterial meningitis were identified from the medical centers subset. 117 had bacterial pathogens defined (Table 1). Hib infection represented 6.84% of all bacterial meningitis cases. We project the proportion of bacterial meningitis cases in the inpatient database to be similar between 1997 and 2000. The number of estimated Hib meningitis cases was 48. The annual incidence of Hib meningitis in patients under 5 years old was calculated to be 3.22 per 100,000 (48/1,489,242) in 2000.

In the data obtained from the medical center database in 1997, all Hib meningitis cases occurred before the age of 2 years and peaked between the ages of 6 months and 12 months. Two-thirds of cases occurred before the age of 12 months (Table 2). In 2000, 2 cases were around 2 years old (24 and 25 months old, respectively) and 5 cases were younger. One case was as old as 50 months. Overall, 58.33% (14/24) of the cases occurred before the age of 12 months; 87.5% (21/24) were younger than 2 years old; and 95.83% (23/24) were younger than 26 months old. There was no significant gender predominance. The peak number of cases occurred in the winter.

Table 1. Case numbers of bacterial meningitis with different etiologies in the medical center database in 1997 and 2000

Category	1997	2000
<i>Haemophilus meningitis</i> (%) (ICD-9 3200)	16 (12.12)	8 (3.94)
Pneumococcal meningitis (%) (ICD-9 3201)	10 (7.58)	13 (6.40)
Streptococcal meningitis (%) (ICD-9 3202)	29 (21.97)	35 (17.24)
Staphylococcal meningitis (%) (ICD-9 3203)	5 (3.79)	11 (5.42)
Other bacterial meningitis classified elsewhere (%) (ICD-9 3207)	0	1 (0.49)
Other specified bacteria (%) (ICD-9 3208)	23 (17.42)	49 (24.13)
Unspecified bacterium (%) (ICD-9 3209)	49 (37.12)	86 (42.36)
Total cases	132	203
Incidence ^a	5.57/100,000	3.22/100,000

Abbreviation: ICD = International Classification of Diseases

^a*Haemophilus influenzae* type b meningitis.

Table 2. *Haemophilus influenzae* type b meningitis case numbers according to age group, gender, and seasons of the year

	Age group (months)							Gender		Seasons			
	0-3	4-6	7-9	10-12	13-24	25-36	37-60	Male	Female	Spring	Summer	Autumn	Winter
1997	1	2	6	2	5	0	0	8	8	3	3	4	6
2000	0	3	0	0	2	2	1	5	3	1	3	1	3
Total	1	5	6	2	7	2	1	13	11	4	6	5	9

Table 3. Neurological sequelae of *Haemophilus influenzae* type b meningitis, 1997 and 2000

	No. of cases (%)
Seizure	4 (16.67)
Hydrocephalus	2 (8.33)
Deafness	3 (12.5)
Death	2 (8.33)
Total	24

According to the recorded outcome, there were 2 fatalities in 1997. Three cases had sequelae of deafness and 2 of them died. There were no fatal cases or incidences of deafness in 2000. Neurological sequelae are listed in Table 3. The claimed medical costs summed to NT\$ 2,552,452 in 1997 and NT\$ 1,166,654 in 2000. The mean claimed cost was NT\$ 154,963 for each case for the particular admission.

Discussion

Our study revealed that the annual incidence of Hib meningitis in Taiwanese children younger than 5 years was 5.57 per 100,000 in 1997. Hib was the second most frequent cause of childhood bacterial meningitis in 1997 in Taiwan, accounting for 19.28% of all episodes. The incidence reported in this study is much lower than in many countries. In the prevaccine era, the incidence rate of Hib meningitis in children less than 5 years old ranged from 15 to 69 cases per 100,000 children less than 5 years old in western countries [1,4,7,8]. In non-western countries the incidence rate ranges from 13 per 100,000 in the Dominican Republic [2] to 60 per 100,000 in Gambia [11].

Hib infection was previously perceived to be less critical in Asia. Some population-based studies conducted recently showed discrepancies among areas in Asia. The annual incidences of Hib meningitis in children younger than 5 years old are 95 per 100,000 in the Philippines [8], 50 per 100,000 in India [4], and 9.8 per 100,000 in Vietnam [12]. Some of these results are comparable or even higher than in the West.

This incidence in our study is similar to recent figures reported from Japan (4.7 cases per 100,000) [3], and Singapore (5 per 100,000) [4] but is slightly higher than the results derived from Nanning, China (1.8 per 100,000) [12]. There is also a low incidence of invasive Hib disease in children less than 5 years old in Hong Kong (2.7 per 100,000) [13]. It is evident that the incidences in Taiwan or other Chinese populated regions are lower than those of many western and non-western countries.

Interestingly, Hib became the fourth most frequent cause of bacterial meningitis in 2000, accounting for only 6.84% of cases. The annual incidence declined to 3.22 per 100,000. Previous studies in the United States [14] and France [15] revealed that Hib meningitis incidence rates were stable without year-to-year variation. Experience in the United States [6] and Spain [16] found that both routine immunization or non-routine but widespread vaccination could significantly reduce the occurrence of invasive Hib disease. Hib vaccine was introduced into Taiwan in 1993 and remained a private sector product. The decline of the annual incidence of Hib meningitis from year 1997 to year 2000 may be attributed to the effect of greater usage of the self-paid Hib vaccine.

In the NHIRD, the cases with the diagnosis of ICD-9 code 3200 represented *Haemophilus meningitis*. From a previous report in Taiwan, more than 97% of *H. influenzae* isolates causing meningitis were type b [17]. It is reasonable to consider the cases with the diagnosis of ICD-9 code 3200 as Hib meningitis.

According to previous reports, areas with a high incidence of Hib disease tended to have more Hib infections in subjects of younger age, mainly in the first 6 months of life [8,18]. In our study, the majority of cases developed their illness before the age of 2 years, but do not show higher proportions in the age group younger than 6 months old. This is compatible with the low incidence of Hib meningitis in Taiwan. There have been variable seasonal patterns of Hib infection [8,14]. Our cases occurred more often during the winter months (from December to February, 9 out of 24 cases)

and may be related to more active viral activity in the winter months.

Seven of 24 cases of Hib meningitis (29.2%) had neurological sequelae, including hydrocephalus, seizure disorder, and deafness. The medical costs calculated here were claimed payments by BNHI for the single admission. They did not include the self-paid charge for that admission, or the medical cost for rehabilitation in those cases with neurological sequelae. The total medical costs caused by Hib meningitis would be higher than we reported.

Widespread usage of antibiotics is a common medical practice in Taiwan. According to Chen et al's study [10], the annual incidence of invasive Hib disease determined by hospital reports and cultural identification was 1.6 per 100,000 children less than 5 years old. However, it is likely that some cases of Hib meningitis could not be diagnosed because of prior antibiotic use. The incidence determined by hospital reports and bacterial culture could be underestimated. Thus, we measured the overall Hib meningitis cases in inpatient database by extrapolation. The 2 problems in our analysis were the appropriateness of this extrapolation and whether proportions of Hib meningitis in medical centers were comparable to that in the whole island. Nevertheless, our estimated incidence rate is similar to the most recent reports from Singapore and Japan. Hence, we believe there might not be major error in this study.

In conclusion, this study indicated that the incidence of Hib meningitis in children younger than 5 years old in Taiwan was 5.57 per 100,000 in 1997 and declined to 3.22 per 100,000 in 2000, possibly due to increased utilization of Hib immunization. The results of this study may be used for economic analysis of the potential impact of universal immunization in Taiwan. NHIRD analysis is a reliable and practical resource for epidemiological studies.

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