

The Causative Organisms of Bacterial Meningitis in Korean Children, 1986 - 1995

Bacterial meningitis remains a serious cause of morbidity and mortality in childhood. Epidemiologic investigations have shown variability in disease risks among different populations and races. In Korea, however, basic epidemiologic information on bacterial meningitis in children is limited. The main purpose of this study was to analyze bacteriologically proven meningitis cases in terms of the relative frequency of causative organisms, mortality rate, and age distribution beyond the neonatal period. Data was obtained from the hospital records who had been diagnosed with bacterial meningitis at 13 general or university hospitals from 1986 through 1995. The patients had at least one positive CSF culture for bacteria. Of 140 cases of CSF culture-proven bacterial meningitis, 46.4% was ≤ 1 year, 62.1% was ≤ 2 years, 81.4% was ≤ 5 years cumulatively. *Streptococcus pneumoniae* was the most common bacteria responsible for 48 (35.0%) of all cases regardless of age, followed by *Haemophilus influenzae* for 48 (34.3%) and *Neisseria meningitidis* for 8 (6.4%) patients. The case fatality rate was 20.0%, 17.1%, and 16.7% for *N. meningitidis*, *S. pneumoniae*, and *H. influenzae*, respectively. In conclusion, the most common organisms of culture-proven bacterial meningitis in the last 10 years have been *S. pneumoniae*, *H. influenzae*, and *N. meningitidis* in order of frequency. Further study should be extended to nation-wide epidemiologic evaluation to show the incidence of bacterial meningitis caused by these three important organisms.

Key Words : Bacterial meningitis, Etiology, Epidemiology, *H. influenzae*, *S. pneumoniae*

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INTRODUCTION

Even with advances in the development of many powerful antimicrobial agents, bacterial meningitis still remains a serious cause of morbidity and mortality in childhood. Many epidemiologic and microbiologic investigations have reported the variability in disease risk in different populations and races. In the USA, *Haemophilus influenzae* was the most common cause of bacterial meningitis, with an annual incidence of 45-67/100,000 children under 5 years of age prior to the routine immunization with *H. influenzae* type b (Hib) conjugate vaccine (1-3). However, in some European countries, the annual incidence of meningococcal meningitis is higher than that of *H. influenzae* meningitis (4, 5). In other parts of the world, few prospective population-based studies on the epidemiology of bacterial meningitis have been carried out (6).

Despite the general consensus of the importance and seriousness of bacterial meningitis in children in Korea, there is little information on the incidence, causative organisms, mortality rate, and age distribution, etc. beyond the neonatal period. Results from several studies in Korea indicate that *Streptococcus pneumoniae* as the cause of bacterial meningitis in children was 24-50%, *Neisseria meningitidis* 15.8-32.6%, and *H. influenzae* 6-21.1% (7-11). However, it should be considered that these studies were carried out in only one or two hospitals in certain geographic areas through retrospective analysis of hospital-based surveillance records, and thus they may not accurately reflect the actual epidemiologic profiles of the disease in Korea as a whole.

One hundred forty patients with bacterial meningitis were analyzed to give more comprehensive information on the epidemiologic profiles of bacterial meningitis in children in Korea.

MATERIALS AND METHODS

The medical records containing the data on bacterial meningitis patients under 16 years of age (excluding 0-28 days of neonates) confirmed by CSF culture were retrospectively analyzed from January, 1986 through December, 1995. Data from thirteen general or university hospitals were included. Eleven hospitals were located in Seoul, and the other two in cities nearby Seoul, both within 50 km; that is, one in Incheon and the other in Suwon. Patients who had positive antigen tests or with CSF findings consistent with bacterial meningitis, but with negative CSF cultures were not included. The following parameters were evaluated: age, organisms identified in CSF culture, and death. Organisms were identified according to standard procedures in each hospital, but bacterial isolates were not subcultured or serotyped.

RESULTS

During the ten years, 140 cases of culture-proven bacterial meningitis were observed in 13 hospitals. Seventy-five patients (53%) were male, and 65 were female, with a male to female ratio of 1.15:1. The overall median age for these patients beyond the neonatal period and below 16 years of age was 17 months. The majority of the patients (114 cases, 81.4%) were 5 years of age or under. Children two years or under comprised 62.1% (87 cases), and one or under, 46.4% (65 cases). The relative frequency of bacterial meningitis shows an inverse relationship with age, except for a minor peak at 9 years of age. Overall the most common organism isolated from CSF was *S. pneumoniae* (49 cases, 35.0%), followed by *H. influenzae* (48 cases, 34.3%) and *N. meningitidis* (9 cases, 6.4%). The category "other" included group B streptococcus (32%), streptococcus (other than group B) (20.5%), coagulase negative staphylococcus (17.6%), *Haemophilus parainfluenzae*, *Salmonella*, and *Klebsiella* species (5.9%) and *Staphylococcus aureus*, *Neisseria* (other than

N. meningitidis), *Enterococcus* and *Moraxella* species (2.9%) (Table 1).

For those one year of age or under, the most common organism was *S. pneumoniae* (21 of 65, 32.3%), followed by *H. influenzae* (19 of 65, 29.2%) and *N. meningitidis* (3 of 65, 4.6%). In children between 1 and 5 years, *H. influenzae* accounts for the majority of organisms (27 of 49, 55.2%). However, for those over 5 and below 16 years the most common organism was *S. pneumoniae* accounting for 17 (65.4%) of 26 cases.

Bacteriologically *H. influenzae* was isolated most frequently in younger patients. Out of 48 cases of *H. influenzae* meningitis 19 (39.6%) were one year of age. The cumulative frequency of *H. influenzae* rose gradually to reach 95.8% for those 5 and under. For *S. pneumoniae*, 21 out of 49 cases (42.9%) were found in children one or under (Table 1).

The summer months of July and August and January had the lowest number of bacterial meningitis. The peak months were March and October. The peak months for *S. pneumoniae* were May, for *H. influenzae* October and for *N. meningitidis* March. There was no definite pattern of periodic or cyclic occurrences of large 'epidemic-like' outbreaks over years, except for a relatively minor peak in 1994.

Information on survival was available in 116 (82.9%) cases. The overall mortality rate was 12.1%. The case fatality rate was 16.7%, 17.1%, and 20.0% for *H. influenzae*, *S. pneumoniae*, and *N. meningitidis*, respectively.

DISCUSSION

The main objective of this retrospective study was to find the relative frequencies of the causative organisms of bacterial meningitis of children beyond the neonatal period and under 16, and thus to provide basic epidemiologic information in Korea. It was not possible with the given data to determine the incidence of bacterial meningitis. The data are in no way comprehensive

Table 1. Age distribution of bacterial meningitis cases according to causative organism, 1986-1995

Age of patient (year)	<i>H. influenzae</i> No. (%)	<i>S. pneumoniae</i> No. (%)	<i>N. meningitidis</i> No. (%)	Other bacteria No. (%)	Total No. (%)
1	19 (39.6)	21 (42.9)	3 (33.3)	22 (64.7)	65 (46.4)
2	13 (27.1)	5 (10.2)	2 (22.2)	2 (5.9)	22 (15.7)
3-5	14 (29.2)	6 (12.2)	1 (11.1)	6 (17.6)	27 (19.3)
6-15	2 (4.2)	17 (34.7)	3 (33.3)	4 (11.8)	26 (18.6)
Total	48 (34.3)	49 (35.0)	9 (6.4)	34 (24.2)	140 (100)

The category "other" included group B streptococcus (32%), streptococcus (other than group B) (20.5%), coagulase negative staphylococcus (17.6%), *Haemophilus parainfluenzae*, *Salmonella*, and *Klebsiella* species (5.9%) and *Staphylococcus aureus*, *Neisseria* (other than *N. meningitidis*), *Enterococcus* and *Moraxella* species (2.9%).

enough to represent the general pediatric population of Korea. The hospitals which participated in this study were either general hospitals or university hospitals; that is, rather selected and high-risk patients are referred to these hospitals from the vicinity as well as from a distance. Furthermore, all the hospitals were in a relatively localized geographic area. Since only culture-proven cases were selected, our data represent only a part of the actual number of cases of bacterial meningitis, and perhaps the true picture of the relative frequencies and incidence of bacterial meningitis in children in Korea would be much different from this. In addition, there may have been under-reporting or mistakes in reporting, thus underestimating the actual values. In spite of these shortcomings, we believe that this study provides important information on some of the basic epidemiologic profiles of bacterial meningitis in children in Korea, considering the fact that all the results of the previous studies had been derived from limited data involving only one or two hospitals.

Although *H. influenzae* is the most common organism causing childhood bacterial meningitis in the reports from western countries, the reported incidence of *H. influenzae* meningitis among children <5 years old varies around 10-fold, from a low of ~20-30 cases/100,000/year in England (4), the Scandinavian countries (12), and the United States (1, 3) to an intermediate incidence of 60 reported from Gambia (13) and to a high of 150-450 among native American (14), Alaska native (15), or Australian native populations (16). In Korea, the Hib meningitis had not been reported as much as suspected. Most clinicians and health administrators in Korea thought that "*H. influenzae* - is not a problem with us". It was the same in Japan (17). The incidence of invasive *H. influenzae* infection in most areas of Japan was reported to be low, and the rarity of the reports of the disease does not seem to be the result of a simple lack of ability of Japanese medical microbiologists to culture *H. influenzae* properly (18, 19). However, some pediatricians in Korea estimate that the real incidence of *H. influenzae* meningitis would probably be higher than the reports. Some cases of *H. influenzae* infection might have escaped detection due to the failure to obtain definitive bacteriologic isolation by culture because of widespread over-use or misuse of antibiotic which can be initiated by primary physicians or by the patients themselves through easy access to all kinds of antibiotics in the drug store.

It is rather surprising to find that *H. influenzae* accounts for almost the same proportion of patients as *S. pneumoniae* for those 1 year of age or under. Adding to our surprise is that it is the most common causative organism for bacterial meningitis in children five years of age and under even in Korea, although we cannot

comment on the actual incidence. In this study for children over five years of age up to 15, *S. pneumoniae* is responsible for the majority of bacterial meningitis in contrast to the United States and western Europe, where *N. meningitidis* is the more common organism (20-22). *N. meningitidis* in our study was the least frequent among the three major organisms of childhood bacterial meningitis in all age groups.

The case fatality rates are slightly higher than the range reported for the developed countries. For *H. influenzae*, the mortality rate was 16.7% in this study, which was lower than that in developing countries (16-35%) (23, 24) and higher than that in many developed countries (1-5%) (25-27). For *S. pneumoniae* and *N. meningitidis*, case fatality rates of 17.1% and 20.0%, respectively, were higher than those in the western world (28).

One of the main questions that should be addressed in epidemiologic studies dealing with bacterial meningitis is the proportion preventable by immunization. The recent introduction of conjugate Hib vaccines will undoubtedly result in a remarkable reduction in the incidence of invasive Hib disease including meningitis in the world and a profound decrease in the incidence of Hib meningitis in a fully immunized population has been reported in the United States from 1993 (29-31). Since 34.3% of all our cases were due to *H. influenzae* and the majority were observed after the age of 2 months, we can assume that by universally administering *H. influenzae* type b conjugate vaccine, we will be able to eliminate nearly one third of childhood bacterial meningitis cases. However, since capsular serotyping of *H. influenzae* isolates was not performed in this study and the exact incidence of Hib meningitis in Korean children is not known, it is difficult to recommend the universal childhood immunization with Hib vaccine without further studies.

The recent development of conjugate pneumococcal vaccine will probably lead to a product covering the most frequently encountered pneumococcal serotypes in the United States and western Europe (32). However, the serotypes commonly found in Korea are somewhat different from those in western countries (33), and it would be very difficult to include all causative serotypes of pneumococci in one conjugate vaccine. As for meningococcal meningitis, the majority of cases are due to group B, for which a good vaccine candidate does not yet exist (34).

In conclusion, we have shown the relative frequency of bacterial meningitis caused by *H. influenzae*, *S. pneumoniae*, and *N. meningitidis*. Bacterial meningitis in children caused by these organisms poses a considerable health problem in Korea in that mostly young children

are victimized with high case fatality rates and well-known serious complications and sequelae. These results should prompt new epidemiologic studies extended to nationwide investigations which would show the true incidence of bacterial meningitis caused by these three important organisms. Perhaps these data could set the ground for the evaluation of the needs and efficacy of the new conjugate vaccines such as Hib conjugate vaccine, which has already been developed, and pneumococcal conjugate vaccine which is under development.

Hospitals which participated in the Korean Pediatric Bacterial Meningitis Study

The study hospitals were Catholic University Medical College, Our Lady of Mercy Hospital, Incheon; Catholic University Medical College, St. Vincent Hospital, Suwon; College of Medicine, Kyung Hee University Hospital, Seoul; Korea University College of Medicine, Hospital, Seoul; Korea University College of Medicine, Gu-Ro Hospital, Seoul; Seoul National University College of Medicine, Seoul National University Children's Hospital, Seoul; Soonchunhyang University College of Medicine, Hospital, Seoul; Yonsei University College of Medicine, Severance Hospital, Seoul; Yonsei University College of Medicine, Yong-Dong Severance Hospital, Seoul; Ewha Womans University College of Medicine, Tongdaemun Hospital, Seoul; Kangdong Sacred Heart Hospital, Hallym University, Seoul; College of Medicine, Hanyang University Hospital, Seoul; and National Medical Center, Seoul.

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