



ORIGINAL ARTICLE

Occurrence of Haemophilus influenzae B meningitis after the implementation of a mass vaccination program

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Abstract

Objective: To evaluate the incidence of Hib meningitis before and after the implementation of a vaccination program in the state of Rio Grande do Sul State, southern Brazil, in 1999.

Methods: This retrospective study summarizes all data concerning Hib meningitis recorded by the state of Rio Grande do Sul Department of Health/Acute Communicable Disease Surveillance Agency between 1995 and 2001. All data were analyzed using the chi-square test (statistical significance: $p < 0.05$).

Results: The decline in the number of cases of Hib meningitis was associated with the Hib vaccine coverage in children. From 1995 to 2001 the incidence of Hib meningitis decreased 89% (from 1.35 cases/100,000 people in 1995 to 0.15 cases/100,000 in 2001 ($p < 0.01$), especially in children younger than 1 year ($p < 0.005$). In the same period, Hib meningitis lethality decreased from 17.8 to 6.7 % ($p < 0.01$).

Conclusions: The implementation of an Hib meningitis vaccination program has nearly eliminated Hib meningitis in the state of Rio Grande do Sul. These findings underscore the need to maintain the vaccination in children, with a thorough investigation of suspected cases and reporting of confirmed cases.

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Introduction

Meningitis represents a significant public health problem, primarily affecting children and adolescents. Notification is compulsory in all suspected cases, irrespective of etiologic agent, and investigation is obligatory, performed by the epidemiological vigilance system. Meningitis caused by *Haemophilus influenzae* b (Hib) has been monitored by the

Health Ministry since 1978. It is endemic all over the country (Brazil) and presents significant variations in incidence when analyzed in different regions and states.

Haemophilus influenzae is classified into six serotypes (a, b, c, d, e, f) according to the different antigens present in its polysaccharide capsule. The non-capsulated form of haemophilus can survive in the airways in a saprophytic form and cause localized infections, in particular sinusitis and otitis (in children) and bronchitis (in adults). The capsulated form, especially type b (Hib), is related to more serious conditions such as meningitis, epiglottitis, pneumonia, cellulitis, septic arthritis, osteomyelitis and pericarditis. Meningitis by Hib has a universal distribution and is a disease that is endemic generally, predominating in temperate climates and during the winter. Its mode of transmission is by means of Flüge's droplets and nasopharyngeal secretions, during the infectious period. The incubation period is unknown, probably varying from 2 to 4 days. Transmission can be established throughout the period in which the microorganism is present, and may be persistent, even without nasal secretions. The illness is no longer transmissible after 24 to 48 hours of antibiotic therapy.¹⁻⁴

Clinically, meningitis by Hib follows a similar course to other types of meningitis, and it is sometimes to distinguish between conditions whose etiology is pneumococcus or meningococcus. Mortality due to meningitis by Hib is greatest in the 0 to 4 years age group, decreasing thereafter.^{1,3-6}

The most specific strategies for the prevention of diseases caused by Hib are immunization programs. In 1988, in the United States (USA), conjugated vaccines were introduced against Hib for children between 18 months and 5 years of age. Since 1990, the Advisory Committee on Immunization Practices has recommended their use throughout American territory, observing that, by 1995, invasive diseases caused by Hib declined by 95%. In 1997, the Pan American Health Organization (PAHO) recommended the routine implementation of vaccination against Hib throughout Latin America, with Uruguay and Chile being the precursors of the process. In September 1999, all over Brazil, the Hib vaccine was implemented for children under 2, in accordance with the National Immunization Program. However, in Londrina and Curitiba, municipalities in the state of Paraná, the introduction of the Hib vaccine occurred 30 months earlier. Compared with the period before vaccination there were significant reductions in the incidence coefficients of meningitis by Hib in Curitiba and Londrina. In the remaining municipalities of Paraná, which did not start vaccination until 1999, these coefficients remained unaltered.^{2,3,7-12}

The objective of this study is to evaluate the impact of the Hib vaccine on the epidemiological status of meningitis within the infant population of the state of Rio Grande do Sul (RS).

Materials and methods

This is a retrospective study which made use of the database containing information on meningitis notifications stored by the Acute Communicable Disease Surveillance Agency of the Rio Grande do Sul Department of Health (ACDSA-DH-RS) referring to the period from 1995 to 2001. This database contains information on all cases of meningitis reported to the Municipal Health Departments, the Regional Health Agencies (CRS) and the ACDSA-DH-RS itself on the Individual Notification Form.

Meningitis is an illness which demands hospital care (First Aid or hospitalization) and, this being the case, the hospitals that are responsible for the majority of data are the locations where an active search for cases should be performed.

In the state of Rio Grande do Sul, suspected cases are reported to the Municipal Health Departments, the Regional Health Agencies (CRS) and ACDSA-DH-RS by means of the Individual Notification Form and investigated following the Individual Meningitis Investigation Form. The epidemiological and laboratory investigation is immediate, adopting disease control measures. The test specimens from suspected cases (cerebrospinal fluid, serum, blood cultures) are sent to the paramount laboratory in the state (LACEN-RS). Later, the results are returned to the regional agencies and from there to the unit that is caring for the patient. The cases are recorded, filed and analyzed, during a first phase, by ACDSA-DH-RS using the National Notifiable Diseases System (SINAN - Sistema Nacional de Agravos de Notificação), in place since 1995.

Following this flow diagram, organized according to the regional division of health activities, information reaches the center where it is analyzed and then divulged. The final results, after epidemiological and laboratorial investigation, return to the CRS and from them to the centers that treat the cases.

The data used for this study was stored as .dbf files and analyzed using the statistical software Epi-Info 6.2 and Tabwin. The chi-square test was applied to analyze differences between the results of certain variables, adopting $\alpha < 5\%$ significance level.

Of all the reports made in RS between 1995 and 2001, only those in which the etiologic agent was Hib were studied. Cases were considered to have been Hib meningitis positive when confirmed by complementary tests (blood culture, cerebrospinal fluid culture, counterimmunoelectrophoresis or latex agglutination).

Incidence coefficients were calculated by 100,000 inhabitants. The population of RS during the study period varied from 9,578,691 in 1995 to 10,183,172 in 2001.

Results

Between 1995 and 2001, 13,924 cases of meningitis were reported in the state of Rio Grande do Sul, of which 31.7% were of viral etiology. The incidence of meningitis has been reducing, especially since 1999, as can be observed in Figure 1. In the specific case of the incidence of meningitis by Hib, this tendency is shown to be greatly accentuated, especially after the implementation of vaccination against this agent within the public health system. In 1995, the incidence of meningitis by Hib was 1.35/100,000 inhabitants, reaching 0.31/100,000 by 2000 and 0.15/100,000 in 2001 ($p < 0.01$). The majority of these cases were diagnosed from cultures (60% in 2001), followed by counterimmunoelectrophoresis and latex hemagglutination.

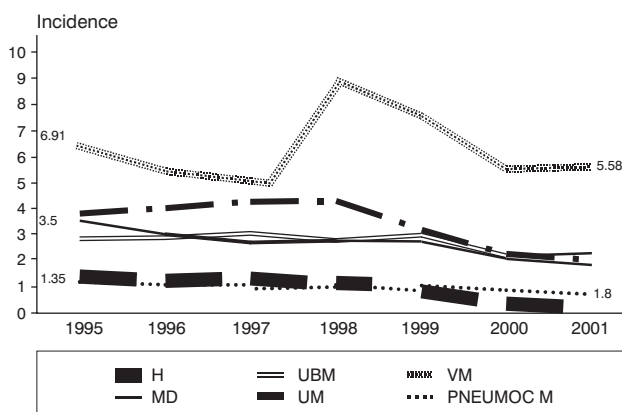


Figure 1 - Cases of meningitis in the state of Rio Grande do Sul: distribution of the incidence coefficients by etiology, 1995-2001

During the period under study, viral meningitis increased from 29.7 to 37.6% proportionally ($p=0.1$), while meningitis of bacterial origin diminished. Meningitis caused by meningococcus were reduced from 15 to 12.1% ($p = 0.4$) and those provoked by pneumococcus were diminished from 4.8 to 4.3% ($p = 0.8$). None of these findings had statistical significance. In contrast, meningitis caused by Hib was significantly reduced from 5.7 to 1% ($p < 0.05$). Figure 2 illustrates the distribution of meningitis between the different etiologies in RS between 1995 and 2001.

Mass vaccination campaigns against type C meningococcus (1995) and type B (1997) had no effect on the incidence of these types of meningitis in RS. The greatest impact was observed on the incidence of meningitis by Hib, which diminished significantly after the introduction of vaccination to the public system in 1999. The lowest incidence rates were reached after 2001 ($p < 0.02$). In Figure 3, incidences of meningitis by meningococcus, Hib and other unspecified bacterial entities in RS, between 1995 and 2001, with the years in which the vaccination campaigns mentioned above were launched are labeled.

Investigating the distribution of Hib meningitis incidence according to age group, reveals that it is greater among children up to 4 years old, and, in particular, in those under 1 year old (Table 1). As can be seen in Figure 4, however, this incidence has been reducing since 1995.

Analyzing the period after the Hib vaccine was introduced to the public system of RS state (after 1999), in Table 1 and Figure 4, it will be perceived that there was a significant reduction in the incidence of meningitis caused by this agent, especially among individuals younger than 1 year (36.5 to 3.4/100,000 inhabitants; $p < 0.005$). In the group of children aged between 1 and 4, the reduction in incidence was also significant (6.4 to 0.7; $p < 0.02$).

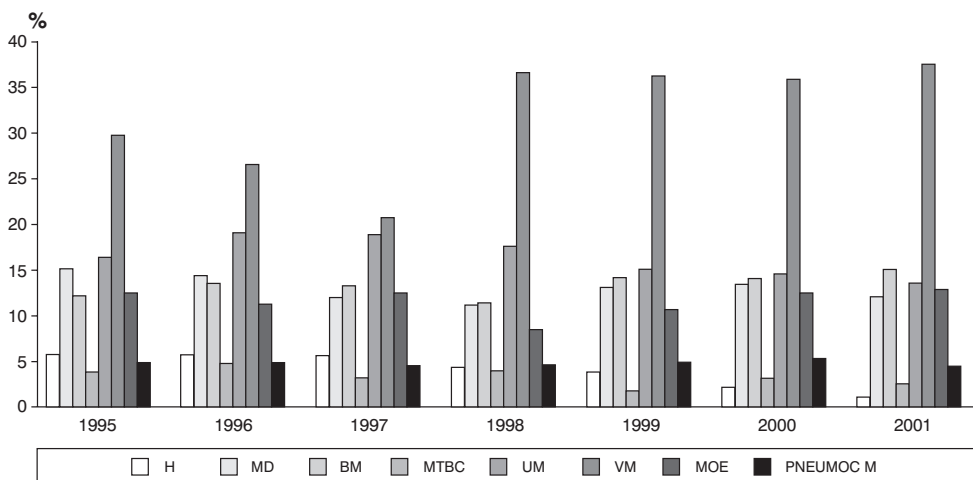


Figure 2 - Distribution of meningitis between the different etiologies in Rio Grande do Sul between 1995 and 2001

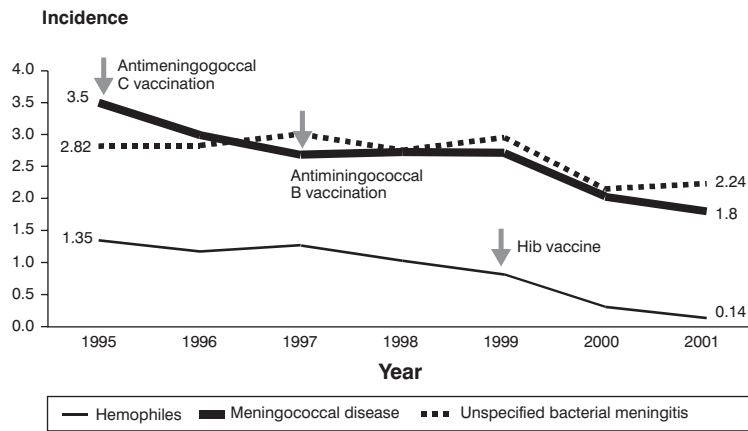


Figure 3 - Incidence of meningitis by meningococcus, Hib and other unspecified bacterial entities in RS, between 1995 and 2001, with the years of antimeningococcal C and B vaccination and Hib vaccination campaigns

Table 1 - Distribution of Hib meningitis incidence according to age group, RS, 1998-2001 (100,000 inhabitants)

Age group (year)	1998	1999	2000	2001
< 1 year	26.9	27.2	8.7	3.4
1 - < 5 years	7.2	4.1	1.7	0.7
5 - < 10 years	0.4	0.3	0.4	0.2
10 - < 15 years	0.1	0.1	0.1	0.0
15 - < 20 years	0.1	0.0	0.0	0.1
> 20 years	0.0	0.08	0.0	0.08

Source: SINAN/RS

In the period that the present study refers to, the lethality of meningitis by Hib in RS, among children less than 1 year old, reduced from 17.8 to 6.7% ($p < 0.01$), as can be seen in Table 2.

Vaccination against Hib on the RS state public health system began in 1999, guaranteeing an improved incidence of meningitis due to that agent. Figure 5 demonstrates the incidence coefficients for meningitis by Hib and the corresponding vaccination coverage for children less than 1 year old in RS since 1995.

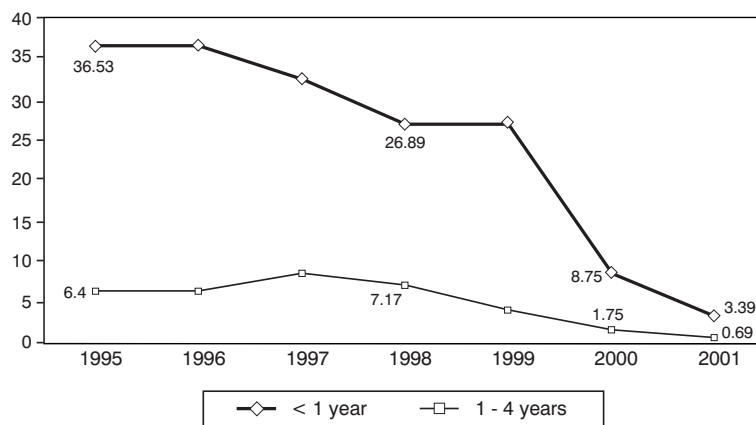


Figure 4 - Hib meningitis incidence in children younger than 1 year and from 1 to 4 years, RS, 1995-2001 (100,000 inhabitants)

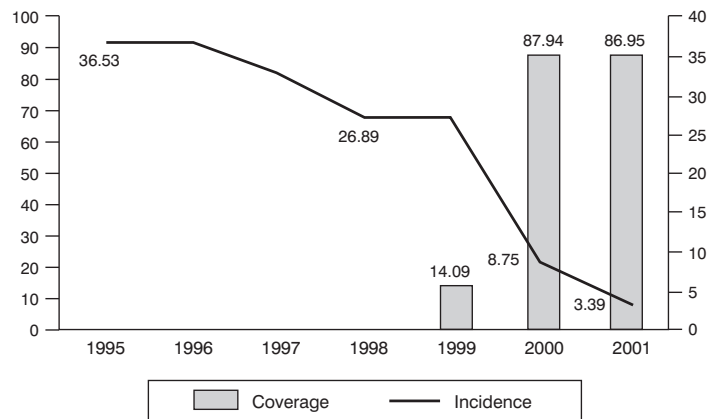


Figure 5 - Incidence coefficients for meningitis by Hib and the corresponding vaccination coverage for children less than 1 year old in RS since 1995

Table 2 - Lethality of meningitis by Hib in RS, among children less than 1 year old, 1995-2001

Year	Lethality
1995	17.83
1996	13.16
1997	10.48
1998	13.73
1999	15.58
2000	9.38
2001	6.70

Source: SINAN/RS

Discussion

Analysis of the data presented should be based on detailed criteria, since epidemiological vigilance within a health system with a municipal structure depends on the quality and experience of the individual centers. This quality varies in accordance with many different factors, in particular, the size of the system, the degree of technical knowledge of the professionals, diagnostic and laboratory support, the routine investigating and divulging results and access to health services.

The incidence of meningitis in RS varied from 23.2 to 14.8 /100,000 inhabitants during the period between

1995 and 2001, with disease forms of viral etiology predominating. Meningitis due to Hib continues to be a significant public health problem, requiring the permanent attention of epidemiological vigilance. Around 10 years ago, all over the world, vaccination against this microorganism was begun. It has become the principal preventative measure against the most invasive clinical form of Hib and especially against meningites.¹¹⁻¹⁵

From 1999 onwards, routine Hib vaccination was implemented for children less than one year old within the public health system of RS. The objective of the vaccination was to achieve 95% coverage of the children within the age group. The data analysis described above shows that after 1999 there was a significant reduction in the incidence and the lethality of meningitis by Hib. It was observed that all bacterial forms of meningitis presented reduced incidence, but with significantly less impact than the reduction in meningitis by Hib. Meningitis from meningococcus, for example, dropped from 15% to 12.1% (NS) and those caused by pneumococcus, from 4.8 to 4.3% (NS). The incidence of meningitis by Hib was reduced almost six fold (5.7% in 1995 to 1% in 2001; $p < 0.05$). Routine Hib vaccination is capable of preventing the colonization of carriers, reducing the number of Hib carriers and, therefore, reduce transmission to susceptible populations. The efficacy of the vaccine is elevated (95-100%), but, its effectiveness does not yet reach 100% of the target population, running at 87 to 88%. According to Center of Disease Control and

Prevention (CDC) recommendations Hib vaccination failures are uncommon events.^{11-14,16}

The reductions observed in the state of Rio Grande do Sul in the incidence of meningitis by Hib after the implantation of vaccination there are similar to reductions demonstrated in a number of different countries, in Europe, North America and Latin America.^{1-4,10,12,17,18} In Brazil, in Londrina, the incidence coefficient of meningitis by Hib was reduced from 23.91 in 1996 to 2.79 per 100,000 inhabitants in 1999, after the introduction of the specific vaccine in the city. A similar situation was established in Curitiba, where the vaccine was also introduced to the public health service. In the remaining municipalities of the state of Paraná, which did not have the vaccine made available, meningitis by Hib incidence indices remained practically unaltered.¹²

With respect of the distribution of meningitis by Hib according to patient age group, it should be pointed out that, in 1965, Turk had already demonstrated that, selecting an asymptomatic population, cultures of oropharynx secretions were Hib positive in 0.4% of adults, 0.8% of children over 5 years old and in 3.2% of those less than 5 years old. This being the case it would appear that Hib carriers predominate in the same age group as the incidence of disease caused by it, which makes congregations (day-care centers, schools, institutions, etc) the foci of health care and vigilance.^{12,13,15,16}

In the present study, cases of meningitis by Hib were confirmed by culture (60% in 2001) and/or counterimmunoelectrophoresis and/or latex particle hemagglutination, which is similar to results found in literature. This demonstrates two essential features of collective health: (a) the quality of diagnosis and of epidemiological vigilance of this disease and (b) the reliability of the data.^{12,18}

The lethality of meningitis by Hib in the state of RS was reduced from 17.8% in 1995, to 13.6% in 1999 and reaching 6.7% in 2001, which is also in agreement with what can be found in other studies.^{1,10,17,18}

In RS, Hib immunization contributed to reduce the incidence of meningitis caused by this agent, resulting in a significant impact of the health of children, particularly those under 1 year. The authors recommend that health professionals should make themselves aware of the epidemiological profile of this disease, with a view to a making early diagnosis possible and that, when necessary, chemoprophylaxis should be started immediately for victims' intimate contacts. In order to improve vigilance it is also important that the number of laboratory diagnoses of bacterial meningitis made by means of cultures and serotyping be increased. Vaccination against *Haemophilus influenzae b* should be continued and guaranteed for the entire pediatric population.

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