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Communication

Surveillance of Bacterial Meningitis in the Italian Hospital of Desio: A Twenty-Year Retrospective Study

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Abstract: Bacterial meningitis is a severe infection with a high fatality rate, and affects children in particular. Three vaccines against the most common bacterial causatives of meningitis, *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, and *Neisseria meningitides*, exist. Monitoring the type and incidence of bacterial meningitis is important for making future prevention and control plans. In this study, we retrospectively analyzed data regarding bacterial meningitis recovered in the Italian Hospital of Desio from 2000 to 2019. Samples from a total of 128 patients were included. *Streptococcus pneumoniae* was the most common microorganism, isolated in 45 cases, followed by *Neisseria meningitidis* (14), *Listeria monocytogenes* (8), *Streptococcus agalactiae* (group B) (4), and *Haemophilus influenzae* type b (2). The implementation of vaccination schedules decreased the number of bacterial meningitis cases caused by *H. influenzae* type b, *S. pneumoniae*, and *N. meningitidis*. Considering the bacterial meningitis cases in subjects aged 0–12 years, no *H. influenzae* type b strain was isolated, five cases of *N. meningitidis* were identified before the introduction of vaccination, and seven *S. pneumoniae* strains were isolated before the introduction of the PCV13 vaccination. Surveillance studies allowed us to monitor changes in bacteria distribution and to guide vaccination strategies.

Keywords: bacterial meningitis; surveillance data; *Haemophilus influenzae*; *Streptococcus pneumoniae*; *Neisseria meningitidis*; vaccine

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1. Introduction

Bacterial meningitis is one of the most relevant worldwide causes of morbidity and mortality, particularly in developing countries, and incidence rates range from 1 per 100,000 individuals per year in high-income countries to 80 per 100,000 subjects per year in low-income countries [1–3]. Bacterial meningitis presents a high fatality rate (up to 20%) that can affect young people, and among infectious agents, such as bacteria, fungi, viruses, and parasites, the most common microorganisms involved are *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, and *Neisseria meningitidis*. In fact, there are three available and effective vaccines against these bacteria, and their epidemiological proportions vary among geographic regions, depending on the vaccination schedule [1,3–6]. Surveillance systems are essential to monitor the distribution of cases, describe the circulating causative organisms, estimate the number of cases that can be prevented, and analyze vaccination failures [1,3,7,8]. The aim of this study was to review bacterial meningitis data recovered in the Hospital of Desio, Italy, from 2000 to 2019, in order to report the circulation of etiological agents and the characteristics of patients involved, thus helping improve surveillance system and vaccination strategies.

2. Materials and Methods

2.1. Study Design and Setting

We retrospectively retrieved data from 128 cases of bacterial meningitis identified in the Hospital of Desio, Italy, from 2000 to 2019. Specimens were collected and analyzed using standard procedures. The identification of bacteria was performed by VITEK® 1 and 2 systems, and from 2014, by VITEK® matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) (bioMérieux, Marcy l'Étoile, France), which used an AXIMA (Shimadzu, Kyoto, Japan) mass spectrometer combined with an open database (SARAMIS v.4.12). Spectrum acquisition was performed using Launchpad software (v.2.9.3). *Escherichia coli* ATCC 8739 was used as a control.

2.2. Statistics

Statistical analysis was conducted on data from confirmed bacterial meningitis cases using the following criteria for inclusion in this study: (I) a laboratory cerebrospinal fluid sample positive for the presence of bacteria; and (II) a meningitis diagnostic code as the principal or secondary diagnosis. All statistical analyses were performed using Stata (Stata Statistical Software: Release 16). A chi-square test was applied to compare results over the study period, which was divided into four intervals of time, 2000–2005, 2006–2010, 2011–2015, and 2016–2019. A p-value < 0.05 was considered statistically significant.

3. Results and Discussion

Of 128 patients with confirmed diagnoses, 20 (16%) were aged < 12 years, with 13 (10%) being younger than 1 year. More than half (58.6%) of study subjects were females. Among individuals aged older than 12, the mean age was 51 ± 25 years. The numbers of bacterial meningitis cases in each five-year period from 2000 to 2019 were 41, 36, 32, and 19, respectively (Figure 1). *Streptococcus pneumoniae* was the most common microorganism isolated, accounting for 45 (35%) cases, followed by coagulase-negative staphylococci (CoNS) (n = 17, 13%), *Neisseria meningitidis* (n = 14, 11%), *Staphylococcus epidermidis* (n = 12, 9.4%), *Listeria monocytogenes* (n = 8, 6.2%), *Streptococcus agalactiae* (group B) (n = 4, 3.1%), and *Haemophilus influenzae* type b (n = 2, 1.6%).

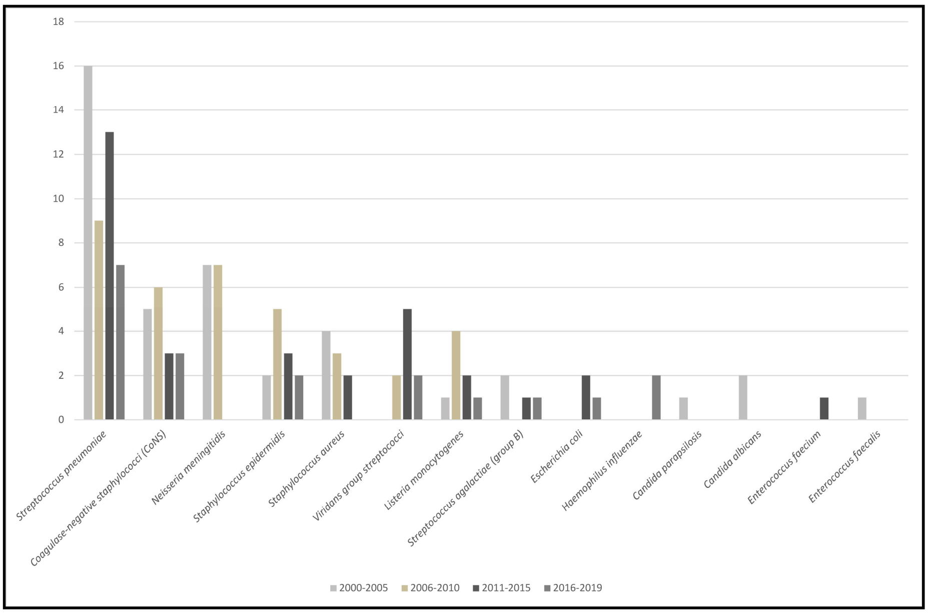

Figure 1. Trends of bacterial isolates from cerebrospinal fluid during the period 2000–2019.

Of the 45 *S. pneumoniae* strains, 7 were isolated in subjects < 12 years, 23 in patients between 13 and 64 years, and 17 in individuals older than 65 years. All 45 pneumococcal isolates were serotyped, and among 26 serotypes identified, the most common were 3 (n = 10, 22.2%), 19A (*n* = 9, 20%), and 12F (*n* = 4, 8.9%), which together accounted for 51.1% of serotyped isolates. In patients aged 5–12, serotypes 1, 12F, 19A, 23B, and 38 accounted for 100% of serotyped isolates, whereas four *S. pneumoniae* strains were isolated from children younger than 5 years. Fourteen *Neisseria meningitidis* strains were isolated, and they were identified during the first two periods, 2000–2005 and 2006–2010. Among these specimens, five cases were isolated in subjects under 12 years (three cases in children < 1 year), seven in patients between 13 and 64 years, and two in individuals older than 65 years. Only two *H. influenzae* type b strains were detected, and they were identified in a 41-year-old man and a 69-year-old woman in the period 2016–2019. Most other bacteria isolated in cerebrospinal fluid were identified in patients affected by pneumonia or urinary tract infections, or in subjects presenting with urinary and peripheral or central intravenous catheters.

S. pneumoniae, *N. meningitidis*, and *H. influenzae* type b, for which vaccines are available, accounted for 48% of meningitis found. There was a significant decrease in bacterial meningitis caused by these three bacteria from the first period, 2000–2005 (*n* = 23), to the last period, 2016–2019 (*n* = 9) ($p < 0.01$). In Italy, since 2017, the National Plan of Vaccination Prevention has included compulsory vaccinations designed to protect children from the following 12 diseases: chickenpox, diphtheria, *Haemophilus influenzae* type b, hepatitis B, meningitis B and C, measles, mumps, polio, rubella, tetanus, and whooping cough [9]. Briefly, diphtheria, tetanus, pertussis, poliomyelitis, *Haemophilus influenzae*, and hepatitis B vaccinations have been mandatory at 3 months, 5 months, 11 months, and 6 years for subjects born since 2001. Second booster doses of diphtheria, tetanus, pertussis, and poliomyelitis have been mandatory at 12–18 years for individuals born since 2001. Varicella vaccination is mandatory in the second year of life and at 6 years in individuals born since 2017. Measles, mumps, and rubella vaccinations are mandatory in the second year of life and at 6 years in individuals born since 2001. Moreover, vaccinations against pneumococcal and meningococcal diseases and rotavirus infection are recommended [9], and since 2000 they have contained capsular polysaccharides from seven serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F). The second and third conjugate vaccines, 10-valent (PCV10) and 13-valent (PCV13), were developed in 2009 and in 2010, respectively. They contain the seven serotypes of PCV7 (4, 6B, 9V, 14, 18C, 19F, and 23F), three serotypes (1, 5, and 7F) of PCV10, and five serotypes (1, 3, 5, 7F, and 19A) and 6A of PCV13. The polysaccharide non-conjugate vaccine PPV23, developed in 1983, contains purified capsular polysaccharides from 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F) and is recommended for adults aged 65 years and older. In Italy, PCV7 was used until 2010, when it was substituted by PCV13. On the other hand, since 2012 the meningococcal vaccination against serogroup C has been available, which includes one dose for children between 13 and 15 months old, four doses against serogroup B for children between 3 and 13 months old, and one dose against tetragroup ACWY for adolescents aged 12–14 years.

Our findings underlined that bacterial meningitis affected all communities, both genders, and all age groups, but there was a decreasing trend over the study period. The implementation of vaccination schedules and the vaccines being mandatory decreased the number of bacterial meningitis cases caused by *H. influenzae* type b, *S. pneumoniae*, and *N. meningitidis*. In fact, considering bacterial meningitis cases in subjects aged 0–12 years during the study period, no *H. influenzae* type b strain was isolated, five cases of *N. meningitidis* were identified before the introduction of vaccination, and seven *S. pneumoniae* strains were isolated before the introduction of PCV13 vaccination, in three of which isolates could not be covered.

It is important to note that meningitis caused by *Streptococcus agalactiae* (group B) was identified in only three cases, most probably due to the introduction of a routine swab test for pregnant women between weeks 35 and 37 to exclude the presence of this bacterium that is associated with invasive infections in neonates.

Reviewing the literature, our data concerning the most frequent etiological agents causing meningitis agreed with results obtained by Giorgi Rossi and coauthors in their monitoring of bacterial meningitis in Lazio, Italy [4], and, similarly, with results reported in different surveillance studies worldwide, such as African regions, Georgia, India, and England [3,5–7,10].

Our study presents some limitations that need to be considered. This study was retrospective and performed in a single center, and a larger number of subjects is required to confirm our results. Furthermore, meningitis caused by CoNS is generally identified in subjects presenting with the implantation of a foreign body or cerebrospinal fluid shunt [11]. Although the availability of clinical data for the first two study periods was limited, our analysis found that cirrhosis, diabetes, alcoholism, tumors, and surgical interventions were associated with CoNS meningitis.

Surveillance studies allow monitoring of vaccination policies and underline the importance of vaccination in the reduction in the number of cases of primary bacterial meningitis, as recently stated by the World Health Organization, which directs the Global Invasive Bacterial Vaccine-Preventable Diseases Surveillance Network with the aim of supporting vaccine introduction and use [8].

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Conflicts of Interest: The authors declare no conflicts of interest.

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