Emerging Problems in Infectious Diseases

Epidemiology of meningococcal disease in the Panamanian pediatric population, 1998-2008

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Abstract

Introduction: Worldwide public health authorities report 500,000 cases of invasive meningococcal disease with 50,000 deaths per year and 10-15% of sequelae in people affected. This study describes the epidemiology, microbiology, and clinical presentation of this disease in the Panamanian pediatric population.
Methodology: The discharge of patients with a meningococcal invasive disease diagnosis was reviewed in the statistical database and archives of the Hospital del Niño.
Results: A total of 32 discharges with a meningococcal disease diagnosis were reported during the study period (1998-2008). Ninety-one percent (n/N = 29/32) were confirmed as meningitis. The mean age of patients was 4.1 ± 4.6 years. The incidence in the period of the study was 0.25/100,000. Infants younger than one year old presented the highest incidence rate and number of cases. Four deaths were reported, three of which occurred in the group of 10-14 years and one in the group of 1-4 years. The overall fatality rate was 12.5%. The serogroup of the causative agent, *Neisseria meningitidis*, was documented in 30 of the 32 cases, with serogroup B the most frequent (66.7%). Ninety-percent (18/20) of serogroup B were isolated in the first five years of study. Serogroup C was identified in 8 of the 12 cases during the period 2004-2008.
Conclusions: The present study showed a change in the epidemiological circulation pattern from serogroup B to serogroup C during the study period**.** Such epidemiological surveillance data is important in the implementation of preventive measures such as vaccination.

Key words: epidemiology, children, *Neisseria meningitidis*, serogroup, Panama

Introduction

Every year meningococcal disease affects more than 500,000 people, with an annual incidence of 1,000 cases/100,000, causing about 50,000 deaths [1,2]. The fatality rate is 10-15% and a wide array of sequelae may occur even in cases adequately managed [1,3]. *Neisseria meningitidis* is a Gram negative diplococcus with a polysaccharide capsule that plays a fundamental role in virulence. Thirteen serogroups have been defined. Serogroups A, B and C are responsible for almost all cases of invasive disease, however, in recent years, an increase of serogroups Y and W135 has occurred [1,3]. Group B strains are generally responsible for epidemic waves with interepidemic periods of variable duration. The strains of group C are generally involved in the production of outbreaks and short-term waves, while serogroup A is fundamentally responsible for major epidemics that cyclically appear in sub-Saharan countries. [1]

The surveillance and reporting of meningococcal disease in Latin America and the Caribbean is heterogeneous and the non-reported cases comprise an amount far from negligible [3]. In the period between 2000 and 2005, there were 6,955 cases reported in different countries to the Caribbean Epidemiology Center. Seventy-eight percent of the cases were reported in Brazil or Chile. Of the total, 69% were serogroup B and 26% serogroup C. Serogroups Y and W135 comprised approximately 2% of the cases [4]. In Panama, according to the SIREVA II regional report, the data recorded show that between the years 2000-2005, serogroup B was responsible for 68% of the cases, with the majority in children younger than 14 years (63.6%) [4]. The most common manifestation was meningitis, with isolation of *N. meningitidis* in cerebrospinal fluid

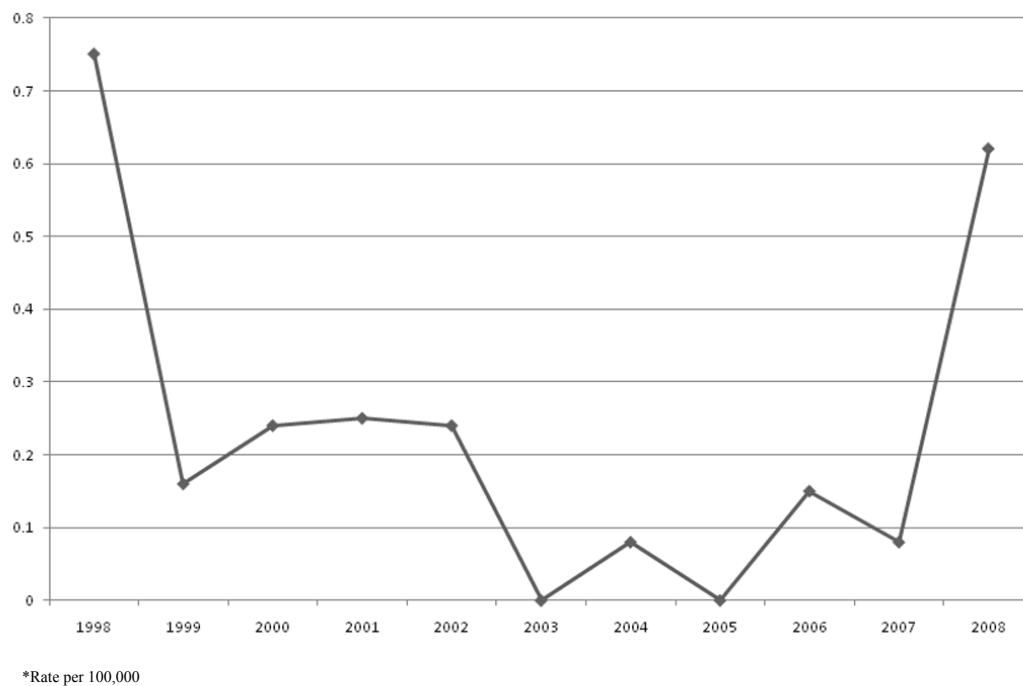**Figure 1.** Hospitalization rate* due to invasive meningococcal disease

*Rate per 100,000

Figure 2. Hospitalization rate per age group due to invasive meningococcal disease
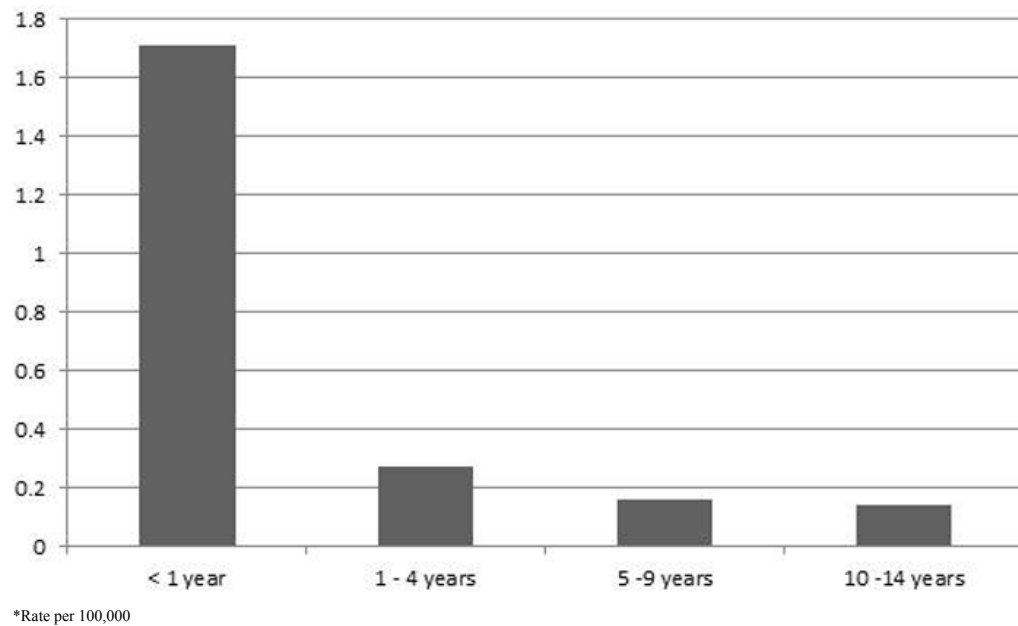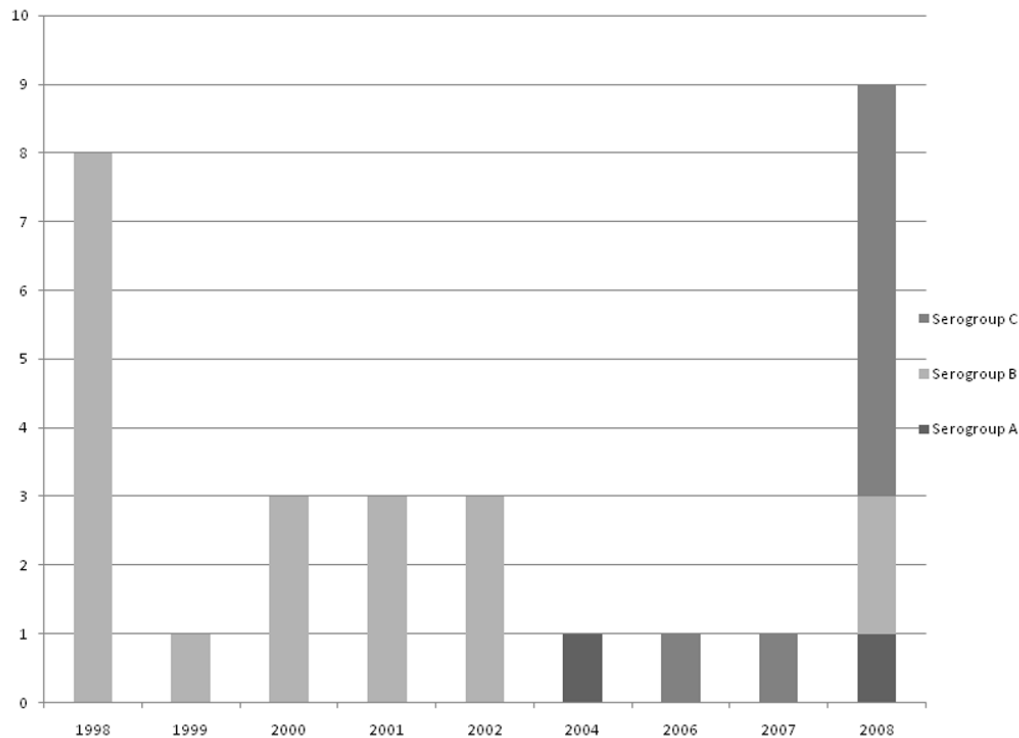

*Rate per 100,000

Figure 3. Distribution of *N. meningitidis* serogroups per year

(CSF) in 95% of cases. Data from 2007 indicate that serogroup C caused 78% of meningococcal disease specifically affecting patients older than 20 years.

Two quadrivalent meningococcal conjugated vaccines have been approved for use in children [5,6]. The serogroup C conjugated vaccine has been routinely used in the United Kingdom since 1999 and is also used in other countries including Spain and Canada, resulting in a reduction in incidence of meningococcal disease [7,8,9]. A vaccine against serogroup B is not available, however, two possible candidates obtained from meningococcal recombinant proteins are under development. The emergence of *N. meningitidis* strains resistant to different antimicrobial agents has been recorded, with resistance to penicillin found in multiple countries [10] and resistance to quinolones reported in North America in recent years [11,12,13].

The purpose of this study was to show the most recent data available on incidence and distribution of meningococcal disease in the Hospital del Niño of Panama.

Methodology

We conducted a retrospective study approved by the Bioethical Committee of the Hospital del Niño, Panama. This study aimed to describe the clinical, epidemiological and microbiological features of meningococcal disease among pediatric patients in Panama**.** The files database of Hospital del Niño were reviewed for discharges of meningococcal disease, in the period between 1 January 1998 and 31 December 2008. Hospital del Niño is the most important third-level hospital in the country, and the national reference center for pediatric patients (0-14 years of age). The hospital has 461 pediatric beds and discharges an average of 19,000 patients per year.

For this study, meningitis was defined as the set of signs and symptoms of inflammation of the meninges with or without petechial or purpuric rash, altered CSF cytobiochemical findings, and microbiological confirmation. Meningococcal septicemia was defined as those signs of sepsis, purpuric rash and microbiological confirmation, with normal CSF. Microbiological confirmation was defined as isolation of *N. meningitidis* from a normal sterile site, and detection of Gram negative diplococci or positive latex agglutination test or PCR from CSF.

For each case, information related to age, gender, dates of admission and medical discharge, days of hospitalization and outcome was extracted. In addition, the administered treatment, antimicrobial

susceptibility testing, serotype of the isolate, and final diagnosis at discharge were analyzed.

The analysis was performed with the SPSS software package (version 16.0 for Windows; SPSS Inc, Chicago, IL, USA). The qualitative variables (gender, diagnosis, and sensitivity to antibiotics) were described in absolute frequency and percentage. The quantitative variables (age, days of hospitalization, treatment duration) were described with means and standard deviation. The data were obtained based on the number of meningococcal cases in the numerator by the general estimated population in the denominator by age group per 100,000 cases.

Results

A total of 32 discharges for meningococcal disease were reported during the study period. Ninety-one percent (29/32) had a diagnosis of meningitis. One patient had a diagnosis of meningitis with bacteremia and two others had sepsis. The mean age was 4.1 ± 4.6 years, and 21 (66%) patients were female. The estimated incidence for the years under study was 0.25/100,000 (Figure 1), with the highest incidence in the group of children under one year of age (1.17/100,000) (Figure 2). Four deaths were reported, three of which occurred in the age group of 10-14 years and one in the age group 1-4 years. All of the deceased patients had a diagnosis of meningitis, and serogroup C was isolated in two of the cases. The overall fatality rate was 12.5%.

Twenty-six isolates were obtained from CSF culture. One case was identified by Gram stain in a CSF smear, and in one other case the diagnosis was made by latex agglutination of CSF. In two cases, a PCR test was used to confirm when the cultures were negative. The serogroup was identified in 30 of 32 cases. Serogroup B was identified more frequently in the first period of time (1998-2002) with only two cases in 2008. Serogroup C was identified in 8 of the 12 cases during the period 2004-2008 (Figure 3). The age distribution of patients with serogroup B isolated was higher in subjects younger than one year (9/20). Patients with serogroup C isolates had a uniform age group distribution.

Information was gathered on antibiotic susceptibility from 17 isolates, specifically, nine of serogroup B, seven of serogroup C, and one non-typeable isolate. Thirteen (76%) of the strains showed susceptibility to penicillin, two strains had intermediate susceptibility (one of serogroup B and serogroup C) and two were resistant to penicillin (serogroup B and C). Resistance to ceftriaxone or quinolones was not reported.

Penicillin was used in the treatment of 52.2% of the cases. Forty percent of the patients received third-generation cephalosporins. Ampicillin, chloramphenicol, fluoroquinolones, and meropenem were other therapeutic options.

Discussion

This study shows the probable epidemiological characterization of meningococcal disease in the Panamanian pediatric population. Since Hospital del Niño is a national reference center and serves 80% of citizens younger than 15 years, we consider that the sample is representative of the country's population. Type B meningococci were associated with most of the cases in subjects younger than five years, which correlates with the literature[14]. The overall fatality rate in the present study was 12.5%, similar to that observed in other series [15,16]. Half of cases corresponded to serotype C, which is in agreement with some other studies [3,17]. In our study, the average incidence was 0.25/100,000. In Latin America the incidence is variable; for example, Mexico reports 0.1 cases/100,000 and Brazil reports two cases/100,000.[3] The present study showed a change in the epidemiological circulation pattern from serogroup B to serogroup C after 2006. Our findings on age distribution coincide with those published by Noronha *et al.* in Rio de Janeiro, where a high rate of attack was reported mainly in children aged less than 12 months, adolescents, and young adults.[18] The cyclical nature of endemic meningococcal disease does not have an accepted explanation. Capsular change is the mechanism by which *N. meningitidis* may modify its capsular phenotype. Meningococcal outbreaks may be started through a capsular change, which is believed to allow an immunological escape of the original serogroup [19,20,21]. It is presumed that this change occurs during the co-colonization of the pharynx with two or more meningococcal strains [22,23] and has been partly responsible for the outbreak due to W-135 in Mecca, Saudi Arabia, with subsequent global dissemination of the endemic strain [24].

Penicillin has been considered for decades the antimicrobial of choice for invasive meningococcal disease. Since 1980, resistant strains have been reported in various regions of the world. Data obtained from the System Monitoring Network, which involved 19 Latin American countries including Panama, monitored bacterial agents

causing pneumonia and meningitis (SIREVA II). This showed that in 2000-2005, 65.7% of isolates were susceptible to penicillin, 34.1% showed intermediate susceptibility and 0.2% were resistant. Regarding our study, more than three quarters of the isolates were susceptible to penicillin; however, data was obtained from only 57% of the isolates, which almost certainly skews the information obtained. Despite this limitation, the use of ceftriaxone as empirical therapy in our institution is recommended until penicillin susceptibility has been determined [25,26]. In our series, resistance to fluoroquinolones was not described; however, resistance to this antimicrobial group has been documented in recent publications in North America [10].

This study provides an overview of the occurrence of meningococcal disease in Hospital del Niño of Panama, a national reference institution. Given the scarcity of publications on meningococcal disease in the Central-America region, these data could be useful as a baseline parameter for the production of a conjugated vaccine that mitigates the morbidity-mortality caused by this pathogen.

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