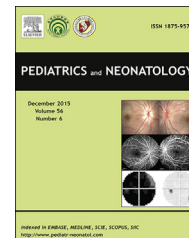


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ORIGINAL ARTICLE

Epidemiologic and Microbiologic Characteristics of Occult Bacteremia Among Febrile Children in Southern Israel, Before and After Initiation of the Routine Antipneumococcal Immunization (2005–2012)

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Key Words

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Kingella kingae;
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 serotypes;
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 vaccine

Background: Little is known about the incidence and dynamics of occult bacteremia (OB) among infants/young children following the introduction of pneumococcal conjugate vaccines (PCVs) into the national immunization program in Israel in 2009–2010. The aim of this study was to characterize the epidemiologic and microbiologic picture of OB among febrile infants/children aged 3–36 months in southern Israel, before and after PCVs introduction.

Methods: Retrospective study enrolling all infants/young children attending the emergency room of a tertiary medical center in southern Israel with fever without source, discharged, and reported with a positive blood culture.

Results: Of 453 true bacteremias, 89 (19.6%) were defined as OB. OB rate was 0.22%; a significant decrease was recorded in OB rates, with the highest rate during 2005 (0.34%) and the

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lowest during 2011 (0.15%). OB cases decreased in post-PCV (2010–2012) versus prevaccination period (2005–2009) from 66/22,256 cases (0.3%) to 23/13,213 cases (0.17%; $p = 0.03$). Most frequent single OB pathogens were *Streptococcus pneumoniae*, *Streptococcus viridans* spp., and *Kingella kingae* (39.3%, 10.1%, and 9.0%, respectively); *Enterobacteriaceae* spp. were isolated in 10 cases (11.2%). No changes were recorded in *S. pneumoniae*-OB cases; *K. kingae*-OB decreased significantly ($p = 0.047$). None of the *S. pneumoniae* serotypes isolated during 2011–2012 belonged to 13-valent PCV (PCV13). An increase in non PCV13 serotypes was recorded during 2011–2012 (3/3, 100% vs. 7/32, 21.9%, $p = 0.01$).

Conclusion: OB rates decreased significantly following the introduction of PCVs. *S. pneumoniae* was the most frequent isolated pathogen in OB, but in lower percentages compared with the medical literature. No PCV13 serotypes were detected as a cause of OB during 2011–2012. Copyright © 2015, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. All rights reserved.

1. Introduction

The definition of fever without source and occult bacteremia (OB) in the daily pediatric practice may differ between various studies and various periods of time, leading to considerable variability in the findings and definitions required at physical examinations and in the calculation of its various incidence rates.^{1–4} Nevertheless, the incidence of OB was relatively constant (2–10%) until the middle of 1980, with a significant decrease following the introduction in the routine practice of vaccination against *Haemophilus influenzae* type b.^{5–8} The introduction of the pneumococcal conjugate vaccines (PCVs) was accompanied by an additional quick and significant decrease in OB cases to rates under 1%.^{9–21} Today, the pathogens expected to be responsible for OB in the era of PCVs are *Neisseria meningitidis*, *Escherichia coli*, *Staphylococcus aureus*, group A *Streptococcus* and *Salmonella* spp., and also nonvaccine serotypes of *Streptococcus pneumoniae*.¹¹ The implementation of the routine vaccination policy with PCV7 in the United States led to a decrease of 84% and 67% in the incidence of the bacteremia caused by *S. pneumoniae* and bacteremia in general, respectively.¹¹

In Israel, PCV7 was introduced in routine use in July 2009 and changed to PCV13 in November 2010. No information is available today either at the national level or in southern Israel regarding the expected changes in the incidence of OB in infants and children aged 3–36 months vaccinated with PCVs, and also on the distribution of pathogens and the therapeutic approach in patients diagnosed with this syndrome.

The main objective of this study was to describe and characterize the epidemiologic, microbiologic, and therapeutic features of OB among febrile children aged 3–36 months treated at the pediatric emergency room (PER) in southern Israel, before and after the introduction of routine PCV vaccination.

2. Methods

This was a retrospective study describing the 8 year period 2005–2012. The Soroka University Medical Center is the only general hospital in southern Israel and provides

primary and tertiary health services to the entire population of southern Israel. It served a population of > 800,000 inhabitants in 2012; of these, > 250,000 were children < 18 years of age. The PER of the hospital accepts around 36,000 visits/y.

In southern Israel, two pediatric populations live side by side: Jewish children, largely urban with a lifestyle comparable to Western populations, and Bedouin children, formerly composed of desert nomads, and now in transition to a Western lifestyle. Hospitalization rates due to respiratory and gastrointestinal infections in general, and invasive pneumococcal diseases (IPDs) particularly, are more prevalent among Bedouin children.^{14,22–24}

Today, all infants in Israel are immunized initially with three doses of *H. influenzae* type b vaccine (at the age of 2 months, 4 months, and 6 months) and two doses of the Prevenar vaccine (Prevenar13 since November 15, 2010, at the age of 2 months and 4 months), followed by a booster with both vaccines at the age of 1 year.

The study population included all infants/young children aged 3–36 months diagnosed in the PER with fever without source, discharged from the PER, and with a positive blood culture (with a true pathogen) reported following the visit.

2.1. Data sources

All of the information was retrieved from medical charts and computerized laboratory data of the study patients. We analyzed the medical records of all patients with a discharge diagnosis of: (1) fever without source; (2) suspected OB; and (3) fever only. Patients with immunodeficiencies, malignancies, and the presence of long-term vascular catheters were excluded. Approval to perform this study was obtained from the IRB of the Soroka University Medical Center.

The treatment protocol in children with suspected OB in the PER required performing blood cultures in every patient aged 3–36 months with a temperature > 38°C. The decision to treat with antibiotic drugs belonged to the treating physician, and was based on presence/absence of a peripheral white blood cell count > 15,000 cells/mm³. In general, even when leukocytosis > 15,000 cells/mm³ was present, there was still a recommendation of refraining from antibiotic treatment if the patient's family was

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