CHARACTERIZATION OF ACUTE OTITIS MEDIA OTOPATHOGENS BEFORE THE INTRODUCTION OF THE PNEUMOCOCCAL CONJUGATED VACCINE INTO THE NATIONAL IMMUNIZATION PROGRAM IN POLAND

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Introduction

- ❖ Acute otitis media (AOM) is the most common cause for antibiotic prescribing to children in the first 5 years of life
- ❖ The main pathogens are *Streptococcus pneumoniae* and *nontypable Haemophilus influenzae* (NTHi).
- ❖ The pneumococcal conjugated vaccines (PCVs) impact on otitis media was significant
- ❖ Thus, understanding the epidemiology of AOM is important to optimize clinical outcomes and promote judicious antibiotic use
- ❖ Bacterial etiologic data for acute otitis media (AOM) otopathogens in Poland are scarce

Methods

Setting

- ❖ The Niekłanska Children's Hospital, in Warsaw, Poland is a 255 beds
- ❖ The pneumococcal conjugated vaccine 10 valent (PCV10) is included in the routine national immunization program in Poland recently but the use of the PCV13 vaccine in the private market is significant.

Study design:

- ❖ Retrospectively over 7 years period (2010-2016)

Case definitions:

Inclusion criteria:

- ❖ Patients visiting the Niekłanska Children's Hospital Pediatric Emergency Room and after hospitalized were enrolled if they
 - ❖ <60 months old
 - ❖ Had AOM as established on the basis of symptoms (pain in affected ear, tugging of the ear, fever, lethargy, or irritation) and signs (erythema, fullness, or bulging of the tympanic membrane)
 - ❖ Had culture obtained from middle ear fluid

Exclusion criteria:

- ❖ Culture was not obtained
- ❖ Data from microbiology laboratory were missing

Database and Statistics

- ❖ Records of all middle ear fluids, were obtained from the microbiology laboratory at Niekłanska Children's Hospital
- ❖ Demographic and laboratory data of children < 5 years old who underwent tympanocentesis due to AOM were obtained from hospital medical records

Laboratory tests for bacterial detection:

- ❖ Pathogenic bacteria in the MEF were identified using standard methods. Briefly, MEF was plated onto the following: Columbia agar with 5% sheep blood; Brain Heart Infusion (BHI) agar or Chocolate agar (for cultivation of *H. influenzae*); MacConkey agar (for cultivation of Gram-negative bacilli); and Chapman agar (for cultivation of *S. aureus*). The MacConkey agar and Chapman agar were incubated at 35–37 °C for 24 h. The BHI agar or Chocolate agar and Columbia agar was incubated at 35–37 °C with 5% CO₂ for 24 h. After the incubation period, identification of bacteria was determined using diagnostic discs and biochemical methods.
- ❖ Antibiotic sensitivity of *S. pneumoniae* was determined using standard discs for oxacillin, erythromycin, clindamycin and sulfamethoxazole-trimethoprim. In the case of oxacillin-resistant strains, the sensitivity to penicillin, ampicillin, cefuroxime, cefotaxime and ceftriaxone was also evaluated by using the strips with the gradient of antibiotic concentrations. Lack of susceptibility to three or more antibiotic classes was considered a multidrug-resistant strain. *S. pneumoniae* isolates were classified as penicillin-susceptible (S, MIC ≤ 0.06 mg/ml), penicillin intermediate-resistant (I, MIC > 0.06–2.0 mg/ml) and penicillin-resistant (R, MIC > 2.0 mg/ml).
- ❖ Antibiotic sensitivity of *H. influenzae* was determined using standard disk with ampicillin, amoxicillin with clavulanic acid, sulfamethoxazole-trimethoprim, penicillin and cefaclor. In the case of penicillin (and/or cefaclor) resistant strains, the sensitivity to ampicillin, amoxicillin with clavulanic acid, cefuroxime, cefotaxime and ceftriaxone was also evaluated by using the strips with the gradient of antibiotic concentrations
- ❖ Antibiotic sensitivity of *Moraxella catarrhalis* was determined using standard disk for amoxicillin with clavulanic acid, cefuroxime, erythromycin, sulfamethoxazole-trimethoprim. The production of beta-lactamase by *H. influenzae* and *M. catarrhalis* was determined with nitrocephin disc. Antibiotic sensitivity of *S. pyogenes* was determined using standard discs with penicillin, erythromycin, clindamycin.
- ❖ Results of susceptibility testing for all bacteria tested were interpreted according to the EUCAST recommendations.

Objective

The aim of this study was to determine the bacterial etiology and antibiotic susceptibility patterns of otopathogens in children prior to the introduction of the pneumococcal conjugated vaccine (PCV) into the national immunization program (NIP) in Poland.

Results

- ❖ Out of 940 MEF cultures, 407 (43.3%) were positive for 419 pathogens
- ❖ The distribution of the pathogens and the proportion of *Streptococcus pneumoniae* (SP) and *Haemophilus influenzae* (Hi) that were antibiotic-resistant are presented in the (Figure 1)
- ❖ No statistically significant differences in distribution of pathogens were observed over time or by age group (<12mo; 12-23mo; 24-59mo).
- ❖ Prevalence of penicillin-resistant SP significantly declined with time (11.3% - 2010-2012; 2.1% - 2012-2014; 0% - 2014-2016), but no significant differences in proportion of resistance to other antibiotics were found (Figure 2)
- ❖ Amoxicillin-clavulanate resistant Hi declined over the 3 time periods (7.7%, 4.2% and 2.0%, respectively), but resistance to other antibiotics did not vary significantly (Figure 3)

Figure 1: Proportion (%) of the various pathogens isolated from the middle ear fluid of 407 culture-positive episodes of children <5 years with acute otitis media before the introduction of the pneumococcal conjugated vaccine into the national immunization program in Poland

Figure 2: Proportion of *S. pneumoniae* resistant to the antibiotic isolated from the middle ear fluid of children <5 years with acute otitis media in Poland

Figure 3: Proportion of *H. influenzae* that were resistant to the antibiotic tested isolated from the middle ear fluid of children <5 years with acute otitis media in Poland

Conclusions

- ❖ This is the largest dataset of otopathogens isolated from middle ear fluid of children <5 years with acute otitis media in Poland
- ❖ Isolates from AOM patients in Poland during the pre-PCV period
- ❖ The most prevalent otopathogen was *S. pneumoniae*, with high rates of resistance to macrolides, clindamycin and oral cephalosporins
- ❖ Penicillin-resistant and amoxicillin-clavulanate resistant *H. influenzae* declined during the study period
- ❖ These data can help to determine the appropriate treatment for AOM and can serve as the baseline before the introduction of PCV to the NIP in Poland