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Risk of childhood otitis media with focus on potentially modifiable factors: A Danish follow-up cohort study

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ABSTRACT

Introduction: Otitis media is the primary cause of antibiotic prescription in children. Two-thirds of all children experience at least one episode of otitis media before the age of 7 years.

The aim of this study was to characterise the attributable effect of several modifiable risk exposures on the risk of > 3 episodes of otitis media at age 18 months and 7 years within a large prospective national birth cohort.

Methods: The study used the Danish National Birth Cohort comprising information about otitis media and risk exposures from more than 50,000 mother-child pairs from the period 1996–2002. Logistic regression models were used to estimate odds ratios for the risk factors and to calculate the population attributable fraction.

Results: Short time with breastfeeding, early introduction to daycare, cesarean section, and low compliance to the national vaccination program were all associated with an increased risk of > 3 episodes of otitis media at 18 months of age and at 7 years of age. The fraction of children with otitis media attributed from breastfeeding lasting for less than 6 months was 10%. Introduction to daycare before the age of 12 months attributed with 20% of the cases of > 3 episodes of otitis media.

Conclusions: Short duration of breastfeeding, early introduction into daycare, cesarean section, and low compliance with the national vaccination program increased the risk of experiencing > 3 episodes of otitis media at 18 months, and at 7 years of age. These are factors that all can be modulated.

1. Introduction

Otitis media (OM) is a common disease during childhood and affects approximately two thirds of all children before the age of 7 years [1]. OM is considered the primary cause of antibiotic prescription for children and adolescents in western countries [2,3]. Although OM is often used to describe an infection in the middle ear, OM does not represent a single disease entity, but instead represents a continuum of conditions from secretory otitis media (SOM), acute otitis media (AOM), to a chronic condition with perforation and hearing impairment.

Thus, OM is an important disease entity in the discussion of antibiotic overprescription and antibiotic resistance. Furthermore, the direct and indirect costs of childhood OM are considerable and estimated at around 233–260 $ in the US [4–6] and up to 575 € in Sweden per episode of OM [7]. With an incidence in Denmark of 624 episodes per 1.000 child-years during the first year of life [8] and up to 39.2% of all children experiencing more than 6 episodes of OM before the age of 7 years [9], OM is a notable health economic burden. Finally, in some severe cases, OM leads to long-term adverse developmental outcomes, thus increasing the individual and societal costs even more.

Prior studies have identified several potential risk exposures in relation to OM. Some factors have consistently been shown to be correlated with increased risk of developing OM, including male gender, multiparity, maternal smoking, short duration of breastfeeding, and early daycare attendance [10–14]. However, recent evidence has challenged some of these established risk factors [15–17].

The aims of our study are threefold: To investigate if previously established modifiable risk factors identified in smaller studies can be identified in a very large nationwide prospective cohort; to unravel their temporal relationship with OM assessed at two distinct time points, at 18 months of age and at 7 years of age; and to estimate fractions of OM cases occurring in the population that might be attributed to exposures to these factors.

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2. Material and method

2.1. Study design

Data were drawn from a large multipurpose cohort study (The Danish National Birth Cohort – DNBC) including 100,329 pregnancies. Prospective data were collected from the women and their offspring during the period 1996 to 2002. About 30% of all eligible pregnant women in Denmark from this period were included in the cohort, corresponding to a response rate of 60% among the invited women [18]. Only women who did not want to carry their pregnancy to term or could not speak Danish well enough to participate were excluded from the cohort. Enrollment occurred at the first contact to the family physician or the midwife at approximately gestational week 12. The mothers were followed with structured telephone interviews at gestational week 12 and 30, and postnatally at age 6 and 18 months of the child. Later follow-ups were conducted by questionnaires at age 7 years of the child. Information on socioeconomic conditions used in this study was collected from the Population's Education Registry (PER), kept by Statistics Denmark [19].

The DNBC has been ethically approved by the Regional Scientific Ethical Committee of Copenhagen and Frederiksberg (*(KF) 01–471/94*), and by the Danish Data Protection Agency under *2004-41-4078*. The present study was approved by the Danish Data Protection Agency (*2012-58-0003*).

The questionnaires and more information on the cohort can be found at http://www.ssi.dk/English/RandD/Research%20areas/Epidemiology/DNBC/Questionnaires.aspx.

2.2. Study population

Eligible children in this study were those from the DNBC whose mothers had completed at least one of the 6- and 18-month interviews or 7-year follow-up questionnaire with information on number of OM episodes. We excluded mothers-child pairs in which the children had congenital malformations of the outer/inner ear, lip-palate cleft, and trisomy 21, because such factors clearly increase the risk of OM [20–23].

2.3. Main outcome

Mothers in the DNBC gave information on OM on each follow-up. The mother was asked at age 6 and 18 months of the child if her child had experienced any episodes of OM. In the 7-year follow-up, the mother was asked if her child had experienced any inflammation of the middle ear since birth, and if so the number of episodes.

The main outcome was scored as a dummy variable according to the reported numbers of OM episodes at 18 months and 7 years into one of the categories: no episodes, 1–3 episodes, or more than 3 episodes. If the mother could not answer or did not wish to answer, the information was considered as “missing”. If there was inconsistency between the reported number of OM episodes at age 6 and 18 months, the child was scored according to the highest OM category reported in the 6-month or 18-month interview.

2.4. Risk factors

A number of factors have been identified as risk factors for OM [10,24–26]. In the present study, the following factors were included; breastfeeding, use of childcare centres, maternal age at child's birth, socioeconomic status, maternal education, parental smoking after birth, birthweight, gender of the child, parity, cesarean section, fish oil supplement, cow milk consumption, household pets, soft drink consumption, use of pacifier and whether the child has been following the national vaccination programme. Socioeconomic status was rated as the highest achieved socioeconomic position of the parents.

2.5. Statistical methods

To establish our models, the risk variables were assessed for internal correlation. The risk variables were tested in a simple regression analysis in groups with related variables representing social, perinatal, smoking and dietary characteristics together with gender and parity against the outcome at 18 months and 7 years separately, making up two models. One for OM at age 18 months, and one for OM at age 7 years. Variables that were significantly associated with the outcome were included in the main multiple logistic regression model as risk variables. Because the data were not suitable for a proportional odds regression model, a dichotomised risk model of the outcomes “episodes of OM ≤ 3” and “episodes of OM > 3” was chosen. Tests for co-linearity with estimation of the Pearson correlation coefficient were performed for independent exposure variables to assure no co-linearity between variables. Also, interactions between breastfeeding and daycare were tested and no interactions between the two were present in the models.

Multiple logistic regression analyses including the same risk variables in the main model were carried out to estimate the risk of OM according to different breastfeeding and daycare scenarios.

Finally, population-attributable fractions (PAFs) were estimated for daycare attendance and time of termination of breastfeeding, with PAF defined as the proportion of disease cases attributed by an exposure, under the assumption that the exposure is causally related to the outcome [27].

The level of significance for all models was set at the 5% level.

All analyses were performed using SAS 9.4 software (SAS institute Inc. Cary, North Carolina).

3. Results

The study population consisted of 35,613 mother-child pairs for whom information existed on OM in the child from both the 18-month maternal interview and the 7-year maternal questionnaire. Additionally 18,936 mother-child pairs were included for whom OM information was available only deriving from the 6-month or 18-month interview, and 14,688 pairs for whom OM information was available only deriving from the 7-year questionnaire. In the population eligible for the 18-month analysis, 225 pairs were excluded and at age 7 years, 166 pairs were excluded (Fig. 1). At age 18 months, 40% of the children had

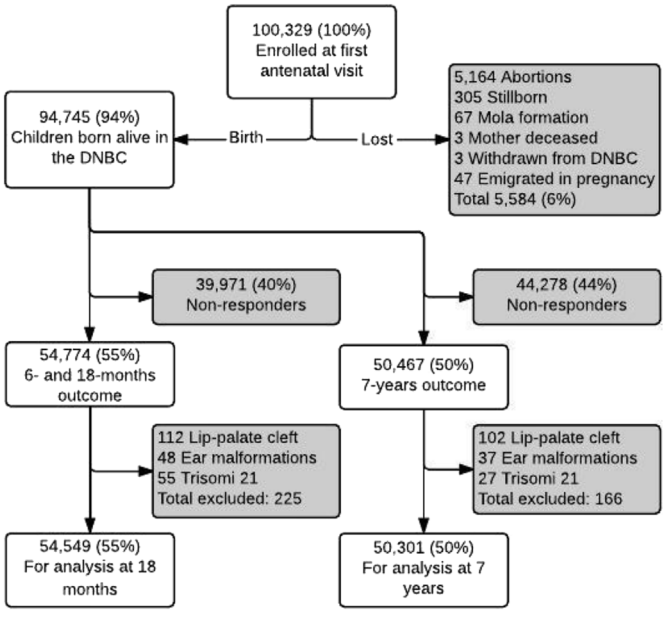

Fig. 1. Flowchart of inclusion and exclusion in the DNBC.