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INTRODUCTION

Otitis media (OM) is a prime reason for doctor consultations, antibiotic prescriptions and surgery in children and causes a significant social and economic burden. Known risk factors for OM include daycare attendance, having older siblings, pacifier use and parental smoking, while breastfeeding reduces risk for OM. Recently, it has been suggested that early life overweight increases the risk of OM later in life.[1,2] Postulated mechanisms include altered expression of pro-inflammatory mediators and Eustachian tube dysfunction due to fat accumulation around its orifice.[1] The evidence to support this association is however limited. The only study published thus far on this topic found that children classified as obese at age 2 months did not have an increased risk of chronic and recurrent OM at age 2 years compared with normal weight children.[2] We aim to provide more robust evidence on this topic by studying the association between body mass index (BMI) at 6 and 11 months of age and the occurrence of OM in the first 4 years of life in a large cohort of Dutch children.

MATERIALS AND METHODS

Study population and setting

This study was performed as part of the Wheezing Illnesses Study Leidsche Rijn (WHISTLER), a large prospective birth cohort study on the determinants of wheezing illness. This study enrolled healthy infants born between 2001 and 2012 in Leidsche Rijn, the Netherlands. Study design and rationale of the WHISTLER study have been reported in detail elsewhere.[3]

Data collection

Information on parental characteristics and prenatal risk factors were collected by a baseline questionnaire. By further monthly questionnaires up to the age of one year data on child characteristics and postnatal risk factors were gathered. Body weight and height were measured during scheduled visits at well-baby clinics. Body height was measured to the nearest 0.1 cm in the supine position using an infant stadiometer, while body weight was measured using an electronic scale and rounded to the nearest 0.01 kg. Data on OM episodes were extracted from the children's primary care electronic health records where all doctor consultations are coded according to the International Classification of Primary Care (ICPC).

Outcome definition

The primary outcome variable was the number of OM episodes in the children's first 4 years of life defined as ICPC codes H71 (Acute Otitis Media; AOM) and/or H72 (Otitis Media with Effusion; OME). Secondary outcomes included the number of AOM and OME episodes separately. A new episode of OM was documented after a disease-free interval of at least 28 days.

Exposure definition

For our exposure primary variable of interest, BMI (weight / height^2) at 6 months, the closest available weight and height data (range 5-7 months) were used. In a sensitivity analysis, we used BMI at 11 months of age (range 10-12 months) as the exposure variable of interest.

Definition of confounders

Sex, prenatal smoking, passive smoking and daycare attendance during the child's first year, parental education, duration of exclusive breastfeeding and having older siblings were considered as confounders and therefore extracted from the questionnaires.

Statistical analysis

First, the incidence of OM, AOM and OME per 100-child years was calculated by dividing the number of OM episodes by the total number of child years. We used negative binomial regression analyses to calculate crude and adjusted incidence rate ratios (IRRs) and accompanying 95% confidence intervals (CIs) for the number of OM, AOM and OME episodes in children's first 4 years of life for each point increase in BMI. Primary care follow-up duration was used as off-set variable to indicate exposure time. Follow-up time was estimated as the time within one of the participating primary care practices from ages 6 months (or 11 months for the sensitivity analysis) up to 4 years or until deregistration from the practice. We only included children registered at participating practices before the age of 6 months and followed up for more than 2 years. Missing values were imputed using the Multivariate Imputation by Chained Equations (MICE) procedure in SPSS. All statistical analyses were performed with SPSS version 20.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

Of the 2,463 children participating in the WHISTLER-cohort study, 1,960 fulfilled the criteria for minimal follow-up and were included in our study (Suppl. Figure 1). Mean weight, height and BMI at age 6 months were 7.8 kg (SD: 0.83), 68 cm (SD: 0.02) and 16.9 (SD: 1.3), respectively. 49% of the children were boys, 77% attended day-care during the first year of life, 52% had older siblings and educational level of parents was high in 76%. During 6,383 child-years of follow-up (mean follow-up per child 3.3 years [SD: 0.5]; median 3.5 years [interquartile range: <0.01]), 2200 OM episodes (2020 AOM and 283 OME, of which 103 were combined AOM and OME episodes) were recorded in 967 (49%) children.

No significant association was observed between BMI at 6 months and the total number of OM, or AOM and OME separately, during the first 4 years of life (adjusted IRR 1.02 [95% CI 0.97 to 1.07]; 1.00 [95% CI 0.95 to 1.06; 1.10 [95% CI: 0.99 to 1.23]). The sensitivity analysis showed that BMI at 11 months of age was neither associated with the total number of OM, AOM or OME during the first 4 years of life (Table 1).

DISCUSSION

Our study performed in a large birth cohort followed prospectively from the age of 6 months shows that BMI at 6 and 11 months of age was not associated with OM occurrence in the first 4 years of life. Our findings are in agreement with the only study addressing the same research question performed thus far.[2] It could however been argued that the timing of assessing obesity in this latter study, at 2 months of age, was too early and the duration of follow-up too short for a reliable assessment of the risk.[2] Furthermore, we analyzed BMI as a continuous variable, as there is currently no universally accepted definition of over-weight and obesity during infancy.

It should be noted that we did not study the inverse relation, i.e. whether early life OM is associated with overweight later in life. Previous studies have suggested that recurrent or chronic OM and related surgery put children at risk for developing overweight and obesity [2,4-7] due to altered chorda tympani nerve functioning which may affect taste and eating habits[8,9].

The major strengths of our study are the large study population and prospective data col-lection. Information bias was minimal since data on OM episodes was collected routinely by family physicians without knowledge of the potential association between OM and BMI. We also included a broad range of potential confounders in our regression models.

Some potential limitations deserve further attention. We primarily used weight and height data at 6 months of age to estimate early life BMI status. As the incidence of OM rapidly increases beyond 6 months of age, we felt that exposure status was best determined at age 6 months to ensure that exposure did actually precede the outcome. However, previous growth studies showed that a BMI during early infancy, especially among those being breastfed, tends to normalize over time. We therefore performed a sensitivity analysis using BMI status at 11 months of age. While one may argue that a potential clinically relevant

association between BMI and OME may have been missed in our main analysis, the sensitivity analysis revealed neither a statistically significant nor clinically important association between BMI and OME.

Furthermore, the educational level of parents participating in our study was relatively high. Although a high social economic status is negatively correlated with BMI, we feel that variation of BMI in our study population was sufficient to detect a potential association between BMI and OM occurrence later in life.

CONCLUSIONS

Early life BMI was not associated with OM occurrence during children's first 4 years of life.

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