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Original Article

Familial risk of sleep-disordered breathing

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ABSTRACT

Objective: To estimate the incidence of hospitalization for paediatric obstructive sleep apnoea syndrome (OSAS) or sleep-disordered breathing (SDB) caused by adenotonsillar or tonsillar hypertrophy without infection in children with a parent affected by OSAS.

Patients and methods: Using the MigMed database at Lund University, hospital data on all children aged 0–18 years in Sweden between 1997 and 2007 (total of 3 million individuals) were used to identify all first hospital admissions for OSAS or either adenotonsillar or tonsillar hypertrophy. Next, individuals were categorized as either having or not having a parent affected by OSAS. Standardized incidence ratios (SIRs) with 95% confidence intervals (CIs) were estimated for boys and girls with a parent affected by OSAS. Children with OSAS or adenotonsillar or tonsillar hypertrophy without a parent affected by OSAS acted as the reference group (SIR = 1).

Results: After accounting for socio-economic status, age, and geographic region, the SIRs of OSAS in boys and girls with a parent affected by OSAS were 3.09 (95% CI 1.83–4.90) and 4.46 (95% CI 2.68–6.98), respectively. The SIRs of adenotonsillar or tonsillar hypertrophy in boys and girls with a parent affected by OSAS were 1.82 (95% CI 1.54–2.14) and 1.56 (95% CI 1.30–1.87), respectively.

Conclusion: This study indicates familial clustering of sleep-disordered breathing, which is important information for clinicians.

1. Introduction

Obstructive sleep apnoea syndrome (OSAS) affects both adults and children with incidence rates of 2–4% [1] and 1–4%, respectively. A recent questionnaire-based epidemiological review suggested that the prevalence of parent-reported symptoms of paediatric sleep-disordered breathing (SDB) is 4–11% [2].

Obstructive sleep apnoea (OSA) is characterized by prolonged partial upper airway obstruction, intermittent complete or partial obstruction, or both prolonged and intermittent obstruction that disrupts normal ventilation during sleep, normal sleep patterns, or both [3,4]. OSAS also includes daytime symptoms. SDB is a wider concept with a spectrum of symptoms in which the milder forms comprise primary snoring and mouth breathing [3,4], often caused by nasal congestion or adenoid hypertrophy. The more severe forms of SDB comprise symptoms similar to the more strictly defined entity, paediatric OSAS (i.e., intermittent breathing pauses [apnoeas], snorts or gasps, and disturbed sleep) [3,4]. In younger children, the most common risk factor for the more severe forms of SDB and OSAS is adenotonsillar hypertrophy [5], and surgical removal of adenoids and tonsils is the first treatment option. Several studies have shown daytime neurobehavioural problems with impaired school performance and hypertension associated with paediatric OSAS and SDB [6,7].

Previous epidemiological studies on familial associations have indicated that genetic factors may constitute a risk factor for OSAS and SDB. In Sweden, the construction of large population-based patient registers led to a previous study by the authors' group that showed increased sibling risk of OSAS and SDB caused by adenotonsillar hypertrophy in children after accounting for socio-economic status, age, geographic region and period of diagnosis [8]. Understanding the familial risk of OSAS or SDB will help clinicians to identify children at risk and offer opportunities for early intervention and treatment.

The present study constitutes a novel contribution as it investigated the relationship between OSAS or SDB with adenotonsillar or tonsillar hypertrophy in children with a parent affected by OSAS.

The aim of this study was to estimate the risk of hospitalization over an 11-year period for OSAS or SDB in children with a parent affected by OSAS. This risk was compared with that of children with OSAS or SDB without a parent affected by OSAS. A further aim was to determine whether there were any differences in age or gender.

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2. Materials and methods

2.1. Outcome variables

The total number of subjects and the incidence of hospital diagnoses of adult and paediatric OSAS, as well as paediatric adenotonsillar or tonsillar hypertrophy, were calculated for different age groups, genders, periods of diagnosis, regions of residence and family incomes. Furthermore, the standardized incidence ratios (SIRs; see below) of the paediatric diagnoses were calculated in children with a parent affected by OSAS and compared with those of children without a parent affected by OSAS.

Sweden has a social welfare system that comprises public primary and hospital health care for all individuals with a residence permit. Sleep studies are required to diagnose OSAS, and full-night polysomnography (PSG) is the gold standard. However, PSG is time-consuming, expensive, and not widely available in all countries. It is generally available in Sweden, but ambulant sleep apnoea recording or polygraphy is more widely used and has been validated against PSG [9]. Sweden follows the definition of OSAS recommended by the American Academy of Sleep Medicine (i.e., apnoea–hypopnoea index [AHI] $\geqslant$ 5 in adults) [4]. There are no strictly defined criteria for paediatric OSAS. However, an AHI of >1 per sleep hour has been proposed [4,10]. Compared with adults, fewer children with OSAS symptoms undergo sleep studies in Sweden; the International Classification of Diseases (ICD) codes included below could therefore represent SDB in the children. Since SDB has no specific diagnostic code, hospitalized children with such symptoms and suspected OSAS are often coded as adenotonsillar or tonsillar hypertrophy instead. Such children are normally referred to an otorhinolaryngological clinic by a primary healthcare or hospital physician. They are mainly admitted to hospital wards for surgical removal of adenotonsillar hypertrophy or, less frequently, for sleep studies. Between 1997 and 2007, approximately 80% of adenotonsillectomies due to SDB were performed in hospitals according to the Swedish National Quality Register for tonsil surgery (A.C. Hessén Soderman, personal communication).

There are several reasons for hospitalization of adults with OSAS (e.g., surgery, treatment with continuous positive airway pressure, and sleep studies).

ICD-10 was used to identify all first hospital admissions for the following outcome variables during the study period (1997–2007) in individuals aged 0–18 years: (1) OSAS, G 47.3; (2) hypertrophy of the tonsils, J 35.1; and (3) hypertrophy of the adenoids and tonsils, J 35.3. Children with a primary diagnosis of upper airway infections (acute tonsillitis, pharyngitis) or milder forms of SDB (only adenoid hypertrophy) were excluded.

The ICD-10 code for OSAS (G47.3) was also used in the parents. Diagnostic codes at the individual level were retrieved from the Swedish Hospital Discharge Register in the MigMed2 database.

2.2. MigMed research database

Data used in this study were retrieved from the MigMed2 database, located at the Centre for Primary Health Care Research, Lund University, Sweden. MigMed is a single, comprehensive database that has been constructed using several national Swedish data registers including, but not limited to, the Population Register, the Multigeneration Register, and the Swedish Hospital Discharge Register (1986–2007) [11–13]. Information from the various registers in the database was linked at the individual level via the national 10-digit civic registration number assigned to each person in Sweden for his/her lifetime. Prior to inclusion in the MigMed database, civic registration numbers were replaced by serial numbers to ensure the anonymity of each individual.

Since the database contains information from the Multigeneration Register, it is possible to link more than 7.6 million index persons (persons born in or after 1932 and registered in Sweden any time since 1961) with their biological parents, children and siblings.

2.3. Explanatory variables

Explanatory variables included gender, age at first hospital diagnosis of OSAS or adenotonsillar or tonsillar hypertrophy, socio-economic status (defined as family income), and geographic region of residence (i.e., in most cases, geographic region of hospitalization). Family income was divided into four categories based on the income level recorded by the taxation authorities.

Family income information was provided by Statistics Sweden and was defined as the family income during the year of childbirth divided by the number of people in the mother's family. The income parameter also considered the ages of individuals in the family, and used a weighted system whereby small children were given lower weights than adolescents and adults.

Geographic region was broken down into large cities (cities with a population of >200,000, i.e., Stockholm, Gothenburg, Malmö), Southern Sweden, and Northern Sweden. Geographic region was included as an explanatory variable to adjust for possible differences between geographic regions in Sweden with regard to hospital admissions for the different outcome variables.

2.4. Statistical analysis

Using the individual-level data in the MigMed2 database, the entire paediatric population of Sweden was sorted into families based on a shared mother and father. The database was then used to determine the presence or absence of a primary hospital diagnosis of paediatric OSAS and/or adenotonsillar or tonsillar hypertrophy in each individual aged $\leqslant$18 years during the follow-up period. Next, the children were categorized as having or not having a parent affected by OSAS. Children with a diagnosis of OSAS or either adenotonsillar or tonsillar hypertrophy but without a parent affected by OSAS constituted the reference group. The individual serial numbers described in the section on the MigMed2 research database were used to ensure that individuals with hospital diagnoses of paediatric OSAS or adenotonsillar or tonsillar hypertrophy only appeared once in the dataset (i.e., for their first hospital diagnosis during the study period).

Person-years were calculated from the start of follow-up on 1 January 1997 to hospitalization for OSAS or either adenotonsillar or tonsillar hypertrophy; death; emigration; or the end of the study on 31 December 2007. Age-specific incidence rates (defined as first hospitalization rates during the study period) were calculated for the entire follow-up period. The results are shown as SIRs with 95% confidence intervals (CIs). SIRs were calculated as the ratio of the observed number to the expected number of cases. The expected number of cases was calculated for age-, gender-, time-period-, region-, and socio-economic-status-specific standard incidence rates derived from children without a parent affected by OSAS. The test statistic χ^2 was used to calculate the probability (*P*-value) of the SIR ratio between boys and girls. Interaction was tested between the age of the child and parental history of OSAS.

2.5. Ethical considerations

This study was approved by the Ethics Committee of Lund University, Sweden.