



Social epidemiology of childhood obstructive sleep apnea



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Abstract

Obstructive sleep apnea is a severe and sometimes life-threatening disorder in childhood and adulthood. During the last decades, its incidence and prevalence rates gradually increase worldwide. The undoubted medico-social significance of the pediatric obstructive sleep apnea stimulates the investigations of this hot topic by scientists from all over the world.

The purpose of this concise review is to outline the most recent achievements in some social epidemiological aspects of the disease. In addition, it deals with the etiopathogenetic role of a series of common accompanying diseases as well as of the numerous risk factors deserving a special attention by the medical community and broad public.

Keywords: obstructive sleep apnea, children, incidence, prevalence, comorbidity, risk factors

INTRODUCTION

Obstructive sleep apnea represents a severe and common disorder in children and adults. When not properly and timely diagnosed and treated it can lead to serious complications. There is a gradual increase of the incidence and prevalence rates of this disease worldwide. The medico-social significance of the obstructive sleep apnea in childhood provokes the intensive research of this hot topic.

The purpose of this concise review is to outline the most recent achievements in some social epidemiological aspects of the pediatric obstructive sleep apnea.

Incidence and prevalence rates of pediatric obstructive sleep apnea

Obstructive sleep-disordered breathing occurs in children of all ages, from newborns to adolescents, with an equal gender distribution in preschool and older children and a peak incidence around 2-8 years (1). It includes habitual snoring with prevalence of 7.45% (range, 3%-35%) and obstructive sleep apnea with prevalence between 2% and 5% (range, 0.1%-13%).

In the general pediatric population, obstructive sleep apnea is present in approximately 2% to 5% of the children (2). In some particular clinical pathologies, however, its incidence can be much higher. The prevalence rates of this heterogeneous disorder vary between 25% and 60% in the children with obesity (3). Obstructive sleep apnea represents one of the most common health problems in the pediatric population affecting between 1% and 4% of all the children in the USA (4). The peak incidence of obstructive sleep apnea in children ranges between two and eight years due to the increased lymphoid tissue size within this age (4).

The results from a systematic review of 30 studies devoted to obstructive sleep apnea prevalence rates among preschool children in the general population demonstrate that prior to 2014, the prevalence varies between 3.3% and 9.4% while during the period between 2016 and 2023, it is higher, between 12.8% and 20.4% (5). In seven studies utilizing the threshold of the apnea-hypopnea index ≥ 5 events/hour, a prevalence rate between 1.8% and 6.4% is reported. In five studies, the implementation of relatively insensitive objective recording methods to confirm the diagnosis of the obstructive sleep apnea estimates a prevalence rate in the range of 0.7%–13.0%.

Obstructive sleep apnea syndrome including snoring and/or sleep apnea is diagnosed in 19 out of a total of 151 children aged between one and 12

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years (in 12.58% of the cases) within a descriptive study in Hospital General Universitario Gregorio Marañón in the city of Madrid, Spain (6). It occurs in 13.5% of the snorers, in 15.1% of the children with sleep apnea, and 15.6% of those with tonsillar hypertrophy.

Comorbidity in pediatric obstructive sleep apnea

Adenotonsillar hypertrophy is the main cause of obstructive sleep apnea in preschool age (between three and five years) (1). The so-called 'congenital-structural' phenotype is characterized by a high obstructive sleep apnea prevalence from the earliest ages of life. It is supported by morpho-structural abnormalities or craniofacial changes and associated with several genetic syndromes such as Prader-Willi syndrome, Down syndrome, achondroplasia, Chiari malformations, and craniofacial abnormalities such as Apert syndrome, Crouzon syndrome, and Pierre Robin syndrome (mandibular hypoplasia). Neuromuscular disorders such as Duchenne muscular dystrophy and spinal muscular atrophy as well as lysosomal storage disturbances are frequently accompanied by a high obstructive sleep apnea prevalence, too.

The prevalence rates of otitis media and other otolaryngologic disorders in children at a mean age of 10.7 ± 4.07 years with obstructive sleep apnea is compared by means of propensity score matching to those without this disease in a large retrospective cohort study in the USA (7). The children with obstructive sleep apnea are by 1.27 times and by 3.86 times statistically reliably more commonly diagnosed with acute and chronic otitis media, respectively ($p < 0.0001$). They undergo statistically significantly more often a tympanostomy (by 3.81 times), an adenoidectomy (by 4.1 times), a tonsillectomy (by 18.2 times), and an adenotonsillectomy (by 24.7 times) ($p < 0.0001$). Allergic rhinitis is statistically reliably by 2.03 times more frequently diagnosed in children with obstructive sleep apnea, too ($p < 0.0001$).

The prevalence rate of otitis media with effusion in 1021 Chinese children with obstructive sleep apnea during the period between January 2019 and December 2020 is investigated (8). Only 73 patients (6.15%) report hearing loss as the main complaint while 178 children (17.43% of the cases)

are diagnosed with otitis media with effusion after the examination. Its incidence rate is higher in obstructive sleep apnea children with adenoid hypertrophy grade IV. Multivariate regression analysis indicates that the younger age (2-5 years), adenoid hypertrophy grade IV, nasal inflammatory disease, and passive tobacco smoking are significant risk factors for both obstructive sleep apnea and otitis media with effusion.

The results from a cross-sectional study in a community cohort of 653 elementary school children in Japan demonstrate associations between the snoring, the severity of obstructive sleep apnea, and the upper respiratory tract infections (9). Multivariable-adjusted odds ratios for these infections are 1.73 (between 1.16 and 2.59 at 95% confidence interval) in children snoring one to four nights per week and 2.82 (between 1.26 and 6.28 at 95% confidence interval) in those snoring ≥ 5 nights per week when compared with never snoring children. Louder snoring is significantly associated with these infections. The odds ratio for these infections in the children with an apnea-hypopnea index ≥ 2.0 events/hour is 2.65 (between 1.32 and 5.31 at 95% confidence interval) when compared with the children with apnea-hypopnea index < 1.0 events/hour.

The prevalence rate of obstructive sleep apnea diagnosed by polysomnography among 136 children with bronchial asthma is 40% (10). Loud snoring, morning dry mouth, and being overweight are associated with obstructive sleep apnea. The combined model of these three features has a positive predictive value of 60.3% and a negative predictive value of 77.6% while the body mass index z-score alone has a positive predictive value of 76.3% and a negative predictive value of 72.2%. This body mass index z-score is useful for obstructive sleep apnea screening in children with bronchial asthma.

Among a total of 263 children diagnosed with obstructive sleep apnea in the tertiary Children's Hospital of Chongqing Medical University in Southwest China during the period between January 2020 and December 2020, there are 51.3% with mild and 48.7% of the cases with moderate to severe symptoms according to standardized guidelines (11). Mild and moderate to severe hypoxemia occur in 39.2% and 60.8% of the cases, respectively. Allergic rhinitis (adjusted odds ratio of 1.75; between 1.03 and 2.96 at 95% confidence interval;



$p < 0.05$) and male gender (adjusted odds ratio of 1.77; between 1.03 and 3.06 at 95% confidence interval; $p < 0.05$) are statistically significantly associated with moderate-to-severe obstructive sleep apnea after adjustment for covariates.

The review of 16 English-language articles published during the period between January 2000 and November 2023 and abstracted in MEDLINE, PubMed, Google Scholar, and Scopus databases reveals an epidemiological association between pediatric obstructive sleep apnea and laryngomalacia (4). Along with adenoid hypertrophy, nasal airway obstruction, and syndromic skeletal anomalies, laryngomalacia is one of the major causes of obstructive sleep apnea in infancy. The percentage of children with these diseases varies between 79% and 14.3% in relation to the children's age. The obstructive sleep apnea is not only a consequence of laryngomalacia but also exacerbates and perpetuates this disorder in infants.

Within a single centre retrospective study of 192 children with Down syndrome at a median age of five years, the prevalence of obstructive sleep apnea diagnosed by overnight polysomnography is 82.3% (12). The obstructive apnea-hypopnea index of 1.5-4.9 events/hour characterizes the severity of the disease as mild, that of 5-9.9 events/hour as moderate, and that of ≥ 10 events/hour as severe. There is mild, moderate and severe form of the obstructive sleep apnea in 27.1%, 19.8%, and 35.4% of the cases, respectively. Age is a statistically significant predictor ($p = 0.012$) for non-rapid eye movement predominant obstructive sleep apnea present in 15.2% of the children with this disease.

The pooled results from the systematic review and meta-analysis of 39 studies including a total of 299358 sickle cell disease patients and retrieved from *Web of Science*, *Scopus*, *PubMed*, *Google Scholar*, and *EMBASE* databases show that more than one half of these patients present with obstructive sleep apnea of different severity (13). The prevalence rates of obstructive sleep apnea among the children with apnea-hypopnea index cutoffs of above 1, 1.5, and 5 are 51% (between 36% and 67% at 95% confidence interval), 29% (between 19% and 40% at 95% confidence interval), and 18% (between 14% and 23% at 95% confidence interval), respectively. Therefore, screening for obstructive sleep apnea symptoms and signs seems useful in sickle cell disease patients.

Risk factors for pediatric obstructive sleep apnea

Obesity which prevalence is progressively increasing and reaching worldwide levels of 5.6% in girls and of 7.8% in boys represents an independent risk factor and regulator of obstructive sleep apnea in childhood (14). There is a bidirectional causal relationship between both disorders. The main factors involved in the association between them are systemic inflammation, oxidative stress, and gut microbiota.

Within an ongoing multicentre, prospective cohort study of 118 children with obesity aged between eight and 19 years, there are 48 obstructive sleep apnea patients (40.67% of the cases) (3). Their mean body mass index is 39.7 ± 9.6 kg/m², their mean age is 14.4 ± 2.6 years, and their mean obstructive apnea-hypopnea index is 11.0 ± 21.1 events/hour. Two clusters are identified and the prevalence of the obstructive sleep apnea is 22.4% and 58.3% ($p = 0.001$), respectively. The children in the second cluster have a statistically significantly higher z-score of the body mass index (4.7 ± 1.1 versus 3.2 ± 0.7); $p < 0.001$), a higher neck-height ratio (0.3 ± 0.02 versus 0.2 ± 0.01); $p < 0.001$) and are older (15.0 ± 2.2 versus 13.7 ± 2.9 years; $p = 0.09$), respectively, than those in the first cluster.

The results from a retrospective study of 921 children aged 2-18 years with polysomnography-diagnosed obstructive sleep apnea show a statistically significant association between a higher body mass index percentile and disease severity ($p < 0.001$; $\rho = 0.15$) (15). The correlation is statistically significant under ($p = 0.007$; $\rho = 0.11$) and over seven years of age ($p = 0.0002$; $\rho = 0.23$). Age is statistically significantly related to obstructive sleep apnea severity ($p = 0.01$; $\rho = 0.08$). Obesity is a significant risk factor for obstructive sleep apnea in younger children, too.

During the period between 2022 and 2023, a prospective cohort study of a total of 5000 children and adolescents aged 3-17 years in a district of Beijing, China, is carried out (16). Of them, 4428 (88.56%) are categorized as low-risk and the rest 572 (11.44% of the cases) as high-risk for obstructive sleep apnea. The children at high risk are more commonly boys than girls (60.0% versus 49.5%), with a family history of metabolic abnormalities (71.5% versus 66.4%), experience passive tobacco

smoking in the past week (37.1% versus 26.6%), and consume sugary beverages daily (7.3% versus 6.8%). Besides they have lower proportions of exclusive breastfeeding in the first six months (55.2% versus 59.7%), normal weight (43.6% versus 58.7%), and normal fat-normal muscle mass (69.7% versus 78.4%). The adjusted odds ratio is 1.53 (between 1.22 and 1.92 at 95% confidence interval) for overweight and 1.94 (between 1.57 and 2.40 at 95% confidence interval) for obesity. Abdominal obesity significantly increases the odds of high obstructive sleep apnea risk (adjusted odds ratio of 1.59; between 1.31 and 1.93 at 95% confidence interval).

The investigation of the population-based Tasmanian Longitudinal Health Study cohort of a total of 3550 individuals reveals that maternal bronchial asthma (odds ratio of 1.5; between 1.1 and 2.0 at 95% confidence interval), maternal tobacco smoking (odds ratio of 1.2; between 1.05 and 1.5 at 95% confidence interval), childhood pleurisy/pneumonia (odds ratio of 1.3; between 1.04 and 1.7 at 95% confidence interval), and frequent bronchitis (odds ratio of 1.2; between 1.01 and 1.5 at 95% confidence interval) are associated with probable obstructive sleep apnea in middle age (17).

The scoping review of 31 papers reveals an association between atopic dermatitis and obstructive sleep apnea in children (18). After adjusting for age, sex, urbanization level, and comorbidities, the atopic dermatitis patients have a higher risk for developing obstructive sleep apnea than controls, with an adjusted hazard ratio of 1.86 (between 1.43 and 2.42 at 95% confidence interval).

The results from the retrospective study in two public hospitals in Hong Kong during the period between September 2017 and November 2019 display an obstructive sleep apnea syndrome risk between 9.5% and 13.6% among 351 Chinese children and adolescents aged between six and 18 years with non-syndromic cleft lip and palate (19). Younger age ($p=0.034$), cleft involving embryonic secondary palate ($p=0.009$), and history of fixed orthodontic treatment ($p=0.002$) are associated with a statistically significantly more common positive obstructive sleep apnea syndrome risk.

Conclusion

Recently, the rising socio-medical significance of the obstructive sleep apnea and, especially, of the pediatric one, provokes a permanent scientific interest worldwide. The issues of the social epidemiology, common accompanying diseases, and crucial risk factors for this disease in childhood require more intensive further interdisciplinary and united large scale research, indeed.

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