

Associations of Sleep Problems with Asthma and Allergic Rhinitis Among Chinese Preschoolers: A Cross-Sectional Study

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Abstract

Background

The aim of this study was to examine the associations of sleep problems with asthma and allergic rhinitis among Chinese preschoolers.

Methods

This cross-sectional survey was conducted in Guangzhou, China. Children aged 3-6 years were selected from 32 kindergartens in 7 regions. Asthma, allergic rhinitis and sleep problem were evaluated by a valid questionnaire. Binary logistic regression models were employed to estimate the odds ratios (OR) and 95% confidence intervals (CI) for asthma and allergic rhinitis according to short sleep duration, late bedtime and frequent nocturnal awakening.

Results

We included 4876 preschool children. Of these, 182 (3.7%) diagnosed as asthma, and 511 (10.5%) diagnosed as allergic rhinitis. Frequent nocturnal awakening was associated with asthma and allergic rhinitis, adjusted OR were 1.49(95% CI: 1.05~2.13) and 1.59(95%CI: 1.27-1.99), respectively. Further subgroup analysis showed the association of frequent nocturnal awakening with asthma differed by gender. No significant associations of short duration and late bedtime with asthma/ and allergic rhinitis were identified.

Conclusions

Our data suggested that frequent nocturnal awakening was associated with asthma and allergic rhinitis, and the association of frequent nocturnal awakening with asthma differed by gender. Further studies are warranted to address the causal relationship between nocturnal awaking and asthma and allergic rhinitis.

Introduction

Allergic respiratory diseases (ARDs), primarily asthma and allergic rhinitis, are important clinical and public concerns all over the world. Globally, asthma and allergic rhinitis affect 4-10% and 10-30% of the whole population [1], respectively. Among children, the prevalence of ARDs is disparity across regions and countries, but the overall prevalence increases year by year [2–4]. ARDs not only increase health and care costs, but also reduce the life quality of suffers [5, 6], which, therefore calling for more preventive measures to minimize its detriment fundamentally.

ARDs are associated with a broad range of environmental factors and lifestyles other than genetic factors [7], which are not fully understood. Recently, associations between sleep problems and ARDs have gained increasing attention. Sleep problems, such as difficulty in settling to sleep, nocturnal awakening, and irregular sleep patterns and short-duration sleep, are common in children. Approximately 25% of children experience some forms of sleep problem during childhood [8]. To date, several studies have examined the association between sleep problems and ARDs. However, there were few studies have been conducted among pre-school age children [9, 10]. In addition, previous studies have suggested that residency in urban areas and prenatal smoking and passive smoking are associated with an increased risk of wheeze and asthma [11–13], however, no study that examined the association between sleep problems and ARDs has adjusted for such confounders. Therefore, the association of sleep problems with asthma and allergic rhinitis among pre-school aged children remains unclear. To identify the association among pre-school age children is substantially important, since pre-school age a critical period for developing the physique and immune system and forming a healthy lifestyle, including developing good sleep habits [10, 14].

The present study aimed to examine the associations of sleep problems with asthma and allergic rhinitis among Chinese preschool children. We hypothesized that sleep problems, include frequent nocturnal awakening, short duration and late bedtime would be associated with ARDs even after adjustment for potential confounders.

Methods

Study design and participants

We conducted a cross-sectional survey of children aged 3-6 years in Guangzhou between July to October in 2015, which was a part of the National Survey on Physical Growth and Development of Children in nine cities of China (NSPGDC) [15]. The NSPGDC used the identical methodology to collect data from nine cities, thus data collected in each city could be analyzed to produce a general conclusion for the local population. The study design, organization, and implementation of the NSPGDC have been published previously [16]. Briefly, in each study city, a cluster random sampling method based on age groups (there were 22 age groups and 150-200 subjects for each sex-age subgroup) for both urban and rural areas was employed to produce a random sample [17]. Children under 3 years in a community was classified as a minimum cluster unit, and children aged 3 and above in kindergarten regarded as a unit. Exclusion criteria included temporary residents, acute illness within a month, chronic illness (such as cardiopathy, chronic nephrosis, tuberculosis, persistent hepatitis), obviously malnourished and physically handicapped.

The data of 3 to 6 years old children in Guangzhou of the survey was included in this analyze. 5102 participants aged 3 to 6 years were selected from 16 kindergartens in urban administrative districts (Yuexiu, Liwan and Haizhu), and 16 kindergartens in rural administrative districts (Conghua, Huadu, Panyu and Baiyun). We excluded 235 participants after reviewing the completeness of the questionnaire (with missing data >15%). Therefore, the remained 4867 participants were included in the final analysis, with an effective response rate of 95.4% (4867/5102). Data was collected by local trained physicians with a structured questionnaire, which include participants' demographic characteristics, mother's health conditions during pregnancy, delivery mode, feeding patterns in the first 6 six months, sleep problems and ARDs of the participants. Body weight and height were also measured by calibrated instruments and standard specifications, and body mass index (BMI) was calculated by dividing the weight in kg by the square of length in m. Age and sex specific BMI z-score was calculated according to the Chinese standard[18].

Measurement

Asthma and allergic rhinitis was assessed by the face to face interviewed questions based on the International Study of Asthma and Allergy in Children Questionnaire (ISAACQ) (*"Has your baby had wheezing or whistling in the chest during the past 12 months?"* *"Has your baby had a problem with sneezing, or a runny, or a blocked nose when he/she did not have a cold or the flu during the past 12 months?"*) [19]. And we asked children's caregivers whether their children had been diagnosed with asthma/allergic rhinitis by doctors in the past 12 months, and whether their children had taken any aerosol inhalation medicine due to the asthma or wheeze? The pediatricians reviewed the questionnaire and made a judgment that children with symptoms of wheeze or whistling in the chest and had been diagnosed with asthma and use asthma medicine in recent 12 months would be defined as asthma, and the children with symptoms of sneezing, or a runny, or a blocked nose and had been diagnosed with allergic rhinitis would be defined as allergic rhinitis.

We assessed sleep duration, usual bedtime and nocturnal awakening frequency during recent two weeks in the present study, using the questions derived from the Chinese version of The Children's Sleep Habits Questionnaire (CSHQ) [20]. Sleep duration was assessed based on the questions (*"Write in your child's usual amount of sleep each day (combining nighttime sleep and naps)."*) According to the National Sleep Foundation's recommendation, preschoolers (3-6years) who sleep less than 10 hours were defined as short sleep duration [21]. Bedtime was assessed by the question (*"write in your child's usual bedtime"*). As the 75 percentiles of bedtime among 3 to 6 aged children in this study was 22:00, the bedtime was classified into 2 groups: at or before 22:00 and after 22:00, and bedtime later than 22:00 was considered as a late bedtime. The nocturnal awakening frequency was assessed by the question (*"write in your child's number of wake up times during the night"*), and classified into 2 groups: none or seldom, and once or more per night. According to the previous study by the National Sleep Foundation [19], children who wakened once or more per night among preschoolers (3-6 years) were defined as frequent nocturnal wakening.

Previous studies suggested a broad range of demographic characteristic and environmental factors that are associated with Asthma and allergic rhinitis [9, 10, 22, 23]. Therefore, we adjusted for these potential confounders, which was distributed differently according to the allergic disease in our analysis, including resident area, age, gender, mother's education, BMI z-score of children, delivery mode, birth weight, maternal tobacco exposure during pregnancy, feeding patterns in the first 6 months.

Ethics declarations

The study was approved by the Ethical Committee for Biomedical Research in Guangzhou Women and Children's Medical Center, and was conducted in accordance with Helsinki

Declaration and Ethical Guidelines for Research Involving Human Participants. A written informed consent was obtained from all the participants' parents before starting of the survey.

Statistical analysis

Mean and standard deviation were reported for continuous variables. Frequencies and percentage were reported for categorical variables. T tests and Chi-square tests were used for comparing continuous and categorical variables, respectively. Binary logistic regression models were employed to estimate the odds ratios (OR) and 95% confidence intervals (CI) for asthma and allergic rhinitis according to short sleep duration, late bedtime and frequent nocturnal awakening, respectively. In each logistic regression model, three models were fitted.

In model 1, we estimated the crude ORs. In model 2, we adjusted for demographic characteristics, included region (urban/rural), gender (boys/girls), age, mother's educational level (college or above/senior high school/junior high school or below) and BMI z-score. In model 3, we additionally adjusted for delivery mode (vaginal delivery/cesarean delivery), birth weight (<2500 g/2500-3900g/≥4000 g), maternal tobacco exposure (smoking or passive smoking) during pregnancy, feeding patterns in the first 6 months of the children (breastfeeding/artificial feeding/mixed feeding), passive smoking (yes/no). We further conducted subgroup analysis to examine whether gender influence the associations of asthma and allergic rhinitis with frequent nocturnal awakening where significant associations were found. Missing data of continuous covariates was inputted based on means and categorical covariates was inputted by the median. Significance level was set at $P < 0.05$ and all tests were 2-sided. Statistical analyses were conducted using SPSS Statistics, version 25.0 (IBM Corp).

Results

Participants' characteristics

We included 4867 children in the current analysis. Of them, 2518 (51.7%) were boys and 2383 (49.0%) were from the urban areas. The mean age of the participants was 4.28 ± 1.05 years. The other characteristics of the participants were summarized in Table 1.

Table 1
The characteristics of the participants

Characteristics		Total (n=4867)	Asthma		Allergic rhinitis	
			Yes(n=182)	No(n=4685)	Yes(n=511)	No(n=4356)
Region	Urban	2383(49.0)	103(56.6) *	2280 (48.7)	283(55.4) *	2100(48.2)
	Rural	2484(51.0)	79(43.4)	2405(51.3)	228(44.6)	2256(51.8)
Gender	Boys	2518(51.7)	93(51.1)	2425(51.8)	300(58.7) *	2218(50.9)
	Girls	2349(48.3)	89(48.9)	2260(48.2)	211(41.3)	2138(49.1)
Age	3 years	1448(29.8)	58(31.9)	1390(29.7)	124(24.3)*	1324(30.4)
	4 years	1381(28.4)	56(30.8)	1325(28.3)	144(28.2)	1237(28.4)
	5 years	1273(26.2)	49(26.9)	1224(26.1)	161(31.5)	1112(25.5)
	6 years	765(15.7)	19(10.4)	746(15.9)	82(16.0)	683(15.7)
Ethnicity	Han	4767(97.9)	178(97.8)	4589(98.0)	503(98.4)	4264(97.9)
	Others	100(2.1)	4(2.2)	96(2.0)	8(1.6)	92(2.1)
Mother's educational level	College or above	3205(65.9)	133(73.1)	3072(65.6)	374(73.2) *	2831(65.0)
	Senior high school	1063(21.8)	29(15.9)	1034(22.1)	83(16.2)	980(22.5)
	Junior high school or below	599(12.3)	20(11.0)	579(12.4)	54(10.6)	545(12.5)
Mother's occupation	Famers	36(0.7)	0(0)	36(0.8)	6(1.2)	30(0.7)
	Workers	1467(30.1)	65(35.7)	1402(329.9)	151(29.5)	1316(30.2)
	Servicer	977(20.1)	33(18.1)	944(20.1)	106(20.7)	871(20.0)
	Others	2387(49.0)	84(46.2)	2303(49.2)	248 (48.5)	2139(49.1)
Family annual income (RMB)	<50000	567(11.6)	15(8.2)	5523(11.8)	58(11.4)	509(11.7)
	~100000	1262(25.9)	46(25.3)	1216(26.0)	125(24.5)	1137(26.1)
	~300000	2292(47.1)	89(48.9)	2203(47.0)	263(51.5)	2029(46.6)
	>300000	746(15.3)	32(17.6)	714 (15.2)	65(12.7)	681(15.6)
Delivery methods	Vaginal delivery	2587(53.2)	94(51.6)	2493(53.2)	249(48.7) *	2338(53.7)
	Caesarean delivery	2280(46.8)	88(48.4)	2192(46.8)	262(51.3)	2018(46.3)
Preterm birth	Yes	134(2.8)	9(4.9)	125(2.7)	19(3.7)	115(2.6)
	No	4733(97.2)	173(95.1)	4560(97.3)	492(96.3)	4241(97.4)
Birth weight (g)	<2500	74(1.5)	5(2.7) *	69(1.5)	9(1.8)	65(1.5)
	2500-3999	4610(94.7)	173(95.1)	4437(94.7)	489(95.7)	4121(94.6)
	≥4000	183(3.8)	4(2.2)	179(3.8)	13(2.5)	170(3.9)
Feeding patterns in the first 6 months	Breastfeeding	1585(32.6)	45(24.7)	1540(32.9)	37(26.8)*	1448(33.2)
	Artificial feeding	873(17.9)	33(18.17)	840(17.9)	101(19.8)	772(17.7)
	Mixed feeding	2409(49.5)	104(57.1)	2305 (49.2)	273(53.4)	2136(49.0)
Maternal tobacco exposure during pregnancy	Yes	1694(34.8)	76(41.8)*	1618(34.5)	194(38.0)	1500(34.4)

* $P < 0.05$

Characteristics		Total (n=4867)	Asthma		Allergic rhinitis	
			Yes(n=182)	No(n=4685)	Yes(n=511)	No(n=4356)
Passive smoking of Children	No	3173(65.2)	106(58.2)	3067(65.5)	317(62.0)	2856(5.6)
	Yes	1969(40.5)	82(45.1)	1887(460.3)	215(42.1)	1754(40.3)
	No	2898(59.5)	100(54.9)	2798(59.7)	296(57.9)	2602(59.7)
Children's BMI z-score		0.09±0.98	0.14±0.97	0.09±0.98	0.03±0.92	0.10±0.99
* P<0.05						

Overall, 182 (3.7%) of the participants were diagnosed as asthma. Compared with the participants without asthma, participants with asthma were more likely to be living in urban areas having low birth weight and exposed to tobacco exposure during pregnancy. There were 511 (10.5%) participants diagnosed as allergic rhinitis. Compared with participants without allergic rhinitis, those with allergic rhinitis were likely to be living in urban areas, boys, cesarean delivery, less breast-feeding and having higher maternal educational level (see Table 1).

Association Between Sleep Problems And Asthma

Of the 4867 children included, 292 (6.0%) had a short sleep duration. Among the children who diagnosed as asthma, 10 (5.5%) had a short sleep duration; while among the children without asthma, 282 (6.0%) had a short sleep duration. No significant association between short sleep duration and asthma was found (Table 2). There were 976 (20.1%) participants go to sleep after 22:00. Among the children who diagnosed as asthma or not, 41 (22.5%) and 935 (20.0%) had late bedtime, respectively. There was also no significant association between late bedtime and asthma (Table 2). There were 816 (16.8%) participants had frequent nocturnal awakenings, 42(23.1%) participants diagnosed as asthma and 774 (16.5%) participants without asthma had frequent nocturnal awakenings, significant association between frequent nocturnal awakenings and asthma was found (Table 2).

Table 2
Frequency and proportion of sleep problems by asthma and allergic rhinitis

Sleep problems	Total(N=4867)	Asthma (n/%)		χ^2	P	Allergic rhinitis (n/%)		χ^2	P
		Yes(N=182)	No(N=4685)			Yes(N=511)	No(N=4356)		
Short Sleep duration									
No	4575(94.0)	172(94.5)	44.3(94.0)	0.09	0.77	470(92.0)	4105(94.2)	4.15	0.04
Yes	292(6.0)	10(5.5)	282(6.0)			41(8.0)	251(5.8)		
Late bedtime									
No	3891(19.9)	141(77.5)	3750(80.0)	0.72	0.40	391(76.5)	3500(80.3)	4.19	0.04
Yes	976(20.1)	41(22.5)	935(20.0)			120(23.5)	856(19.7)		
Frequent Nocturnal awaking									
No	4051(83.2)	140(76.9)	3911(83.5)	5.40	0.02	395(77.3)	3656(83.9)	14.41	<0.001
Yes	816(16.8)	42(23.1)	774(16.5)			116(22.7)	700(16.1)		

The unadjusted and adjusted ORs for asthma for sleep problems were showed in Table 3. From model 1 to model 3, the ORs were not change substantially. In the fully adjusted models, significant association was only found between frequent nocturnal awakenings and asthma, the OR was 1.49(95% CI: 1.05~2.13). Further subgroup analysis showed that significant association between frequent nocturnal awakenings and asthma was found among girls but not among boys (Table 4).

Table 3
Association of sleep problems with asthma or allergic rhinitis among per-school children

	Model 1^a	P	Model 2^b	P	Model 3^c	P
	OR (95%CI)		OR (95%CI)		OR (95%CI)	
Sleep problems and asthma						
Short Sleep duration						
No	1(Ref)		1(Ref)		1(Ref)	
Yes	0.91(0.47-1.74)	0.770	0.98(0.50-1.89)	0.940	0.95(0.49-1.84)	0.867
Late bedtime						
No	1(Ref)		1(Ref)		1(Ref)	
Yes	1.17(0.82-1.66)	0.396	1.12(0.78-1.60)	0.535	1.11(0.78-1.58)	0.574
Frequent Nocturnal awaking						
No	1(Ref)		1(Ref)		1(Ref)	
Yes	1.52(1.07-2.16)	0.021	1.50(1.05-2.13)	0.026	1.49(1.05-2.13)	0.028
Sleep problems and allergic rhinitis						
Short Sleep duration						
No	1(Ref)		1(Ref)		1(Ref)	
Yes	1.43(1.01-2.01)	0.043	1.26(0.89-1.80)	0.197	1.23(0.86-1.76)	0.247
Late bedtime						
No	1(Ref)		1(Ref)		1(Ref)	
Yes	1.26(1.01-1.56)	0.041	1.25(1.01-1.56)	0.045	1.24(0.99-1.54)	0.056
Frequent Nocturnal awaking						
No	1(Ref)		1(Ref)		1(Ref)	
Yes	1.53(1.23-1.91)	<0.001	1.59(1.27-1.99)	<0.001	1.59(1.27-1.99)	<0.001
a Model 1: Unadjusted;						
b Model 2: Adjusted for region, gender, age, mother's educational level, and BMI z-score.						
c Model 3: Additionally adjusted for delivery mode, birth weight, and maternal tobacco exposure during pregnancy, feeding pattern before 6 months.						

Table 4
Association between frequent nocturnal awaking and asthma according to gender

Frequent nocturnal awaking	No. of asthma	Model 1 ^a	<i>P</i>	Model 2 ^b	<i>P</i>
		OR (95%CI)		OR (95%CI)	
boy					
No (N=2086)	73(3.5)	1(Ref)		1(Ref)	
Yes (N=432)	20(4.6)	1.34(0.81-2.22)	0.259	1.35(0.81-2.24)	0.253
girl					
No (N=1965)	67(3.4)	1(Ref)		1(Ref)	
Yes(N=384)	22(5.7)	1.72(1.05-2.82)	0.031	1.68(1.02-2.78)	0.042
a Model 1: Unadjusted;					
b Model 2: Adjusted for region, gender, age, mother's educational level, BMI z-score, delivery mode, birth weight, maternal tobacco exposure during pregnancy, feeding pattern before 6 months.					

Association Between Sleep Problems And Allergic Rhinitis

Among participants diagnosed having allergic rhinitis, 41 (8.0%) had short sleep duration, 120 (23.1%) had a late bedtime, and 116 (22.7%) had frequent nocturnal awakenings, respectively; while among participants without allergic rhinitis, 251 (5.8%) had short sleep duration, 856 (19.7%) had a late bedtime, and 700 (16.1%) had frequent nocturnal awakenings, respectively. Significant associations of short sleep duration, late bedtime and frequent nocturnal awakenings with allergic rhinitis were found (Table 2 and Model 1 in Table 3). However, significant association was only found between frequent nocturnal awakenings and allergic rhinitis after adjusted for potential confounders (Table 3). In the fully adjusted model (Model 4), the adjusted OR for allergic rhinitis for frequent nocturnal awakenings was 1.59(95%CI: 1.27-1.99). And the association between frequent nocturnal awakenings and allergic rhinitis was found both in boys and girls. (Table 5).

Table 5
Association between frequent nocturnal awaking and allergic rhinitis according to gender

Frequent Nocturnal awaking	No. of allergic rhinitis	Model 1 ^a	<i>P</i>	Model 2 ^b	<i>P</i>
		OR (95%CI)		OR (95%CI)	
boy					
No (N=2086)	232(11.1)	1(Ref)		1(Ref)	
Yes (N=432)	68(15.7)	1.49(1.11-2.00)	0.007	1.57(1.17-2.12)	0.003
girl					
No (N=1965)	163(8.3)	1(Ref)		1(Ref)	
Yes(N=384)	48(12.5)	1.58(1.12-2.22)	0.009	1.73(1.15-2.30)	0.006
a Model 1: Unadjusted;					
b Model 2: Adjusted for region, gender, age, mother's educational level, BMI z-score, delivery mode, birth weight, maternal tobacco exposure during pregnancy, feeding pattern before 6 months.					

Discussion

In this study, we used a representative citywide survey data, which was part of the NSPGDC, to investigate the association of sleep problems with asthma and allergic rhinitis among children aged 3-6 years in Guangzhou. The results revealed the prevalence of

asthma and allergic rhinitis among preschool children was 3.7%, and 10.5% respectively. The findings also suggested that frequent nocturnal awakenings but not short sleep duration and late bedtime, was significant associated with asthma and allergic rhinitis. However, these associations of frequent nocturnal awakenings and asthma differed by gender.

In the present study, we found that the prevalence of asthma and allergic rhinitis among preschool children was consistent with previous studies conducted both in some region and countries. For example, Deng's research in Beijing among preschool children revealed the prevalence of doctor-diagnosed childhood asthma was 2.8% [24], Pereira et al conducted study in Portuguese children aged 3-5 years demonstrated that the prevalence of physician-diagnosed asthma was 4.6%, and prevalence of physician-diagnosed rhinitis was 11.8% [25]. Deng and colleague's research in Changsha in China exhibited the prevalence of ever doctor-diagnosed allergic rhinitis was 7.3% [26]. Although Bloom's research in UK showed the prevalence of preschool wheeze requiring attendance to a physician in 2017 was 7.7%, but only one fifth of the received an asthma diagnosis [27]. However, our results was lower than the average prevalence of six representative cities in China, which showed the prevalence of asthma and allergic rhinitis among preschool children were 8.0% and 16.6%, respectively [28]. As the regional difference, the prevalence of asthma and allergic rhinitis was variant in different regions, and our result was consisted with the Urumqi's prevalence, with 3.5% and 10.9% respectively [28]. The discrepancies among researches might be related to different characteristics of study participants (residence, ethnicity) apart from the different measurements for asthma and allergic rhinitis. Besides, the under-diagnosis although with symptom may underestimated the prevalence of asthma and allergic rhinitis [27].

Our findings suggest that frequent nocturnal awakening was associated with asthma (OR=1.49, 1.05-2.13) and allergic rhinitis (OR=1.59, 1.27-1.99), which were similar to previous studies that investigated the association of sleep problems with allergic diseases among children and adolescent [9, 10, 29]. Wang *et al* conducted a study to examine the associations of sleep disorders with the risk of wheeze and allergic rhinitis among 566 Chine toddlers and found that having more than 2 times of nocturnal awaking per night was associated with a higher risk of wheeze (OR=6.16, 1.28~29.74) [9]. Kozyrskyj *et al* analyzed the conditions of 2398 children from on a community-based birth cohort in Australia and found that persistent nocturnal awakening before 3 years of age was associated with an increased risk of non-atopic asthma at age 6 (OR=1.87, 1.08~3.25), after adjusting for other risk factors of asthma, including co-sleeping, wheeze and family stress [10]. Jernelöv *et al* present data from a longitudinal study showing that children's overtired at the age of 8 years increases the risk of rhinitis symptoms at age 13 [29].

The association between frequent nocturnal awaking and asthma and allergic rhinitis could be explained from two aspects. On one hand, the nocturnal awaking may be consequence of asthma or allergic rhinitis, as the airway inflammation and congestion or the nasal obstruction, may cause them to wake up frequently. There were increasing evidence among children showed the high prevalence of nocturnal awakening caused by asthma or allergic rhinitis [30–32]. On the other hand, the frequent nocturnal awaking may be a risk factor for asthma or allergic rhinitis, which was demonstrated in a longitudinal study [10]. The possible biological mechanism was as follow: first, frequent nocturnal awakening may increase the levels of pro-inflammatory cytokines and decrease the immunologic tolerance to allergen [9, 10], shifting the balance between Th1 and Th2 cytokines towards an allergy related (Th2) pattern [29], which are known factors contributing to allergic diseases such as asthma and allergic rhinitis. Second, frequent nocturnal awakening could disrupt the regulation of the hypothalamic–pituitary–adrenal (HPA) axis [33, 34] and the circadian rhythms of melatonin [35, 36], which showed blunted cortisol awakening response and lower cortisol levels and a decline in the level of melatonin [33, 34], and increase the risk of asthma and rhinitis [37–40]. In summary, the association between frequent nocturnal awakening and asthma and allergic rhinitis might work in both direction. However, as our study is a cross-sectional study, we can't ascribe causality of the association of frequent nocturnal awaking and asthma and allergic rhinitis, further research to address the causal relationship between sleep problems and allergic diseases seem warranted.

In this study, we also found that the associations of frequent nocturnal awakening with asthma was differed by gender, and the association was found only in girls. There was few study detecting the gender difference of association between sleep problems and allergic disease among preschooler in general population. And our result was consisted with the research on asthma patient. For example, Strunk's research on asthma patients in children showed that night awakening caused by asthma was marginally less for males than females [30], Goldstein and colleagues' research among 2-15 years old children revealed that the association of asthma with sleep-disordered breathing was found only in girls [41]. The gender differences may be driven by hormonal effect on school-age children [42]. However, it is noticed that the sex difference of sex hormonal will not be significant, until the onset of puberty [43]. So, whether the explanation can applied to preschoolers still need to verify by the further studies.

Strengths And Limitations

For this citywide cross-sectional study, we recruited 4867 representative participants from rural and urban Guangzhou by using a well-designed protocol, which makes our results more generalized. In the analysis we have adjusted for several important confounders, such as region and maternal tobacco exposures during pregnancy, which was not adjusted in previous studies, making our results more robust. Additionally, there were few study explored the association of sleep problems with asthma and allergic rhinitis among Chinese preschool children in a large sample size, and there was no study explored the gender difference of the association in general population, which will enrich the research in this area.

There were several limitations in our study. First, asthma and allergic rhinitis were not determined by objective measures, but rather parent reported symptom from ISAACQ and previous diagnosis, which although was highly recognized for its reliability and validity and was used in previous studies [10, 29, 44]. Second, sleep problems were assessed through questionnaires based on the parents' reports, instead of objective measurement, thus recall bias may exist. On balance, previous studies have demonstrated that information regarding sleep garnered from parents is likely to be reliable [45]. Third, although we have adjusted for various potential confounders, we did not adjust for family allergy history of the parents or mother's stress during pregnancy, which are risk factors for allergenic diseases [10]. Fourth, this study is a cross-sectional study, which deduces a weak association in the exploration of the causal relationship of sleep problems and asthma and allergic rhinitis. Future prospective research studies are needed to validate these findings, since asthma and allergic rhinitis are significant clinical and public concerns.

Sleep problems including shortened sleep duration, late bedtime and frequent nocturnal awaking are common among children, which have a broad impact on children's development and physical health. In the present study, we used data from the NSPGDC to investigate the association of sleep problems with asthma and allergic rhinitis among Chinese preschool children and found that frequent nocturnal awakening was associated with asthma and allergic rhinitis, and the association of frequent nocturnal awakening with asthma differed by gender. The results suggests that pediatricians should consider evaluating sleep problems when evaluating the consequence or risk factors for asthma and allergic rhinitis, and that parents should help their children developing good sleeping habits to reduce the risk of asthma and allergic rhinitis.

Conclusions

Findings from this well representative study suggested that frequent nocturnal awakening was associated with asthma and allergic rhinitis, and the association of frequent nocturnal awakening with asthma differed by gender. Further studies are warranted to address the causal relationship between nocturnal awaking and asthma and allergic rhinitis.

List Of Abbreviations

ARDs: Allergic respiratory diseases

BMI: Body mass index

CI: Confidence intervals

NSPGDC: National Survey on Physical Growth and Development of Children in nine cities of China

OR: Odds ratio

Declarations

Data Availability Data and material of this study could be available through contacting with the corresponding authors. Data of NSPGDC can't be available because its' intellectual property belongs to Guangzhou Health and Family Planning Commission.

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Authors' contribution YM participated in the conceptualization of this study, acquisition of data, statistical analyses and drafted the main manuscript. JT participated in the statistical analyses and interpretation analyses and review the manuscript. YQW: participated in the statistical analyses and interpretation analyses and revised the manuscript. YH: participated in the acquisition of data and statistical analyses. JJJ participated in data clean and interpretation analyses. LJ and YFX participated in investigation, entering data and review the manuscript. YYS participated in the acquisition of data.

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