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Investigation of the association between sleep problems and food allergies in preschool children with/without siblings: a cross-sectional study in Chongqing, China

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Conflict of Interest
There are no financial or other issues that might lead to a conflict of interest.

ABSTRACT

Purpose: This study investigated the association between sleep problems and food allergies (FAs) in Chinese preschoolers and assessed whether there is a difference in this association among children with/without siblings.

Methods: A cluster-stratified sampling approach was employed to select four districts in Chongqing based on demographic considerations. A total of 16 kindergartens (n = 966 parents) participated in this study. Parents completed the Children's Sleep Habits Questionnaire (CSHQ) and a standard FAs questionnaire. Analysis of covariance and multiple logistic regression were used to assess the associations between sleep problems and FAs after adjusting for relevant confounders.

Results: The study found that 16.3% of children had FAs, with eggs, shellfish, and fruit being the most common allergenic foods. The prevalence of FAs was significantly higher in single children (20.63%) than in children with siblings (13.36%). A total of 70.39% of children had CSHQ scores above the clinical cut-off for sleep disorder. Factor analysis revealed five underlying dimensions from the CSHQ. Factor scores, except for the 'difficulty morning waking' factor, were not significantly different between the two groups. Remarkably, the factor scores of 'parasomnias' and 'sleep anxiety' were significantly higher when children had both siblings and FAs. For all subjects, the odds ratios (ORs) of FAs significantly increased with the presence of sleep disorder (OR, 2.35; 95% confidence interval [CI],1.50–3.68) and 'difficulty falling asleep' (OR, 1.34; 95% CI, 1.22–1.48). The subgroup analysis showed that the probability of FAs significantly increased with the 'difficulty falling asleep' (OR, 1.32 vs. 1.38) and sleep disorder (OR, 2.48 vs. 2.14) in children with and without siblings, respectively. The 'parasomnias' was positively associated only with children with siblings.

Conclusion: This study suggests that children with siblings might be more susceptible to FAs when accompanied by certain sleep problems. Further studies are warranted to address the underlying dimensions and possible mediation effects of having siblings with sleep problems.

Keywords: sleep disorder; food allergies; preschool children; siblings

INTRODUCTION

Previous studies pointed out that up to 50% of children would experience sleep problems [1,2]. As it is known that sleep problems can alter children's immune regulation, sleep problems increase the risk of relevant allergic diseases [3]. Children with respiratory and atopic diseases experience poorer sleep than healthy children without [4]. Furthermore, a frequent nocturnal awakening had been associated with asthma and allergic rhinitis among preschoolers [2].

Food allergies (FAs) are immune-mediated adverse reactions to ingested food that can result in a range of symptoms, including respiratory, skin, digestive, and cardiovascular symptoms. FAs can be classified into different grades of severity, and in rare cases, the occurrence of anaphylaxis can lead to death within minutes [5]. FA has also been suggested to involve mental problems, especially in children and adolescents [6]. In recent years, FAs have recently emerged as another allergy epidemic following allergic rhinitis and asthma [7]. Globally, peanuts, milk, and eggs are the most common causes of FAs in children, accounting for up to 80% of cases [7,8]. A study within a pediatric referral practice noted that more than 70% of children's FA cases were towards multiple foods. However, there is no definitive cure for FAs, and patients must rely on avoiding allergenic foods and emergency treatments for accidental ingestion, which can be challenging and may result in unintended adverse reactions [5].

Worldwide, FA has a 6% to 8% prevalence rate in children [9] and has been recognized as a challenge for public health problems that also affect the daily lives of children and their caregivers to varying degrees [10]. FAs are also considered to be a neglected "hidden killer" of food safety in 2020, China [11]. The emergence of FA cases has been alarming, and researchers are beginning to understand the possible reasons for such an increase [12], such as the relationship between FAs and sleep problems. It was reported that children with gastrointestinal (GI) FAs were commonly associated with poor sleep [13], and eczema and FAs were found closely associated with sleep disorders [14]. Also, the presence of a FA in a child may be associated with a deterioration in sleep quality [15]. Wang [16] et al. reported that snoring and nocturnal waking were associated with increased odds of having FAs in Chinese infants.

China is moving to an aging population; the Chinese government has enacted a 3-child policy [17], which is expected to increase the number of multiple-child families. However, Chongqing's average number of household members per household was 2.45, down from 2.70 in 2010 [18]. Evidence shows that early childhood illnesses, older siblings' presence, and furred pets in the household all influence the likelihood of developing allergy disorders via changed microbial exposure [19]. Recent research has demonstrated a positive correlation between the presence of siblings and an increased incidence of sibling conflict, which is associated with reduced sleep duration and increased total sleep problems in children [20]. We hypothesized that perhaps the presence of siblings might affect the relationship of sleep to FAs.

Preschool (3 to 6 years of age) is known to be a critical period for developing the physique and immune system and also forming a healthy lifestyle such as the development of good sleep and food intake habits [21]. The prevalence of sleep problems experienced by children in western China was reported to be significantly higher than in Eastern areas [22]. Chongqing is a western city in China, where the prevalence of FA in children aged under two years was reported to rapidly increased after the 1990s and gradually stabilized after 2010 [23].

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However, literature regarding the relationship between FAs and sleep problems among preschool-aged children, especially in West China seems scarce. Therefore, this study aims to explore whether sleep problems are associated with FAs in Chinese preschoolers and whether the associations could be different among children with siblings compared to single children when the potential effect of significant confounders are controlled.

METHODS

Design and study subjects

This is a cross-sectional survey conducted by stratifying random sampling. Concerning the prevalence of FA (11.1% in 2019) in Chongqing [23], the target sample size (n = 914) was determined using G Power (version 3.1.9.6), with a statistical power of 0.95, a significance level of 0.5, and an effect size g of 0.04 at two-tailed. Additionally, we set a 5% non-response, and a minimum of 956 cases were required to be included as research objects in this study.

A cluster-stratified sampling approach was employed to select 4 out of the 8 districts in Chongqing based on geographic location, economic level, and population density. Two kindergartens were selected from each district, resulting in a total of 1,267 preschoolers. Among them, 90% of the caregivers (n = 1,134) consented to the face-to-face questionnaire interviews during parent meetings held at the kindergartens between late January and early February 2021. This study received approval from the Ethics Committee of Chongqing Collaborative Innovation Center for Functional Food in Chongqing University of Education (202102001HS). Exclusion criteria included preschoolers born through cesarean section (n = 148), those with household furred pets (n = 14), and those with a family history of allergies (n = 6). A total of 966 validated data were included in the final analysis.

Measurement

The face-to-face survey questionnaire included three parts of information pertaining to demographic characteristics, FAs, and sleep problems.

Demographics information

The gender, age, height, and weight of preschoolers were collected. Additionally, information was obtained on the main caregivers (i.e., parents, grandparents, and maternal grandparents), siblings, parents' education levels, household income, and family structure. The preschoolers were divided into 2 age groups (the age of 3–4, and the age of 5–6). Education level was categorized as follows: low level including primary school, and junior middle school; medium level including senior high school, vocational/technical, secondary school, and junior college; and higher level including senior college and university. Household income was categorized as follows: a low level if monthly household income was less than 5,000¥, a medium level for more than 6,000¥ but less than 12,000¥, and a high level for more than 12,000¥. The family structure included the nuclear family, the stem family, and others.

The Kaup Index is known to be used to assess the body fullness and nutritional status of preschoolers [24]. We calculated the Kaup index using the subjects' height and weight and then categorized them into three groups, underweight, normal, and overweight.

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FAs

FA information was collected by questions relating to specific FAs, including any anaphylactic reactions based on a questionnaire from a previous study in China [16]. Parents were asked to answer the allergic symptoms that appeared after taking any specific food in the past 12 months, and those whose children experienced FAs symptoms were requested to list causative foods. The original answers include more than twenty food items such as milk, eggs, fish, crab, oyster, shrimp, cashew nuts, peanuts, tree nuts, wheat, soy, peach, orange, mango, beef, mutton, and others. We classified these food items into the nine types of foods or food groups based on previous studies on FAs commonly reported in kindergarteners in China [25,26], which included eggs, shellfish, milk, soy, wheat, beef and mutton, fish and shrimp, fruits, and nuts (peanuts and tree nuts).

Sleep problems

Sleep problems may be categorized into behavioral sleep problems (e.g., sleep anxiety, sleep onset delay) and medical sleep problems (e.g., obstructive sleep apnea, narcolepsy) [27]. In this study, sleep problems were estimated by the Chinese Mandarin version of the Children's Sleep Habits Questionnaire (CSHQ). The CSHQ is a 33-item parent-report instrument encompassing 8 of the original subscales: bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night-time awakenings, parasomnias, sleep-disordered breathing, and daytime sleepiness. A 3-point Likert scale was used to give a rating of 1 for 0–1 nights/week (rarely), 2 for 2–4 nights/week (sometimes), and 3 for 5–7 nights/week (often). A higher score indicated more severe sleep problems and a total score > 41 has been indicates the most sensitive clinical cut-off for identifying probable sleep disorders in children [27]. Other researchers reported that the CSHQ turned out to be a more reliable scale after certain items of daytime sleepiness, pertaining to night-time awakenings and sleep duration were omitted using the exploratory factor analysis in a study of urban Chinese preschoolers [28,29]. We therefore conducted an exploratory factor analysis to obtain underlying dimensions from the CSHQ in this study.

Statistical analysis

All the data were double-entered using EpiData (version 3.02; EpiData Association, Odense, Denmark), and all statistical data were analyzed using Stata statistical software (version 17.1; Stata, Cary, NC, USA). Descriptive statistics were applied to depict characteristics of sociodemographic variables and distributions of FAs with frequency and percentage measures. The statistics of the categorical variables were analyzed using the χ^2 test. The total scores and each summed score of underlying dimensions of the CSHQ were compared using analysis of covariance (ANCOVAs), with demographic factors (child's age, sex, parental education, family structure, and household income) as covariates.

To determine the underlying dimensions, an exploratory factor analysis (EFA) was conducted. The EFA considered both the sleep behavior problem indices and symptomatology of sleep disorders used in devising the original CSHQ. Factors were retained if eigenvalues were greater than one. Both orthogonal and oblique rotations were conducted based on results in the existing literature [29]. The established factor model was then adjusted based on modification indices and residual correlations, with those items with a total coefficient lower than 0.35 deleted.

Multiple logistic regressions were conducted to investigate the associations between sleep problems and FAs for all subjects, with adjustment for the effects of potential confounders. Further subgroup logistic regressions were conducted to assess whether the association

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were differed with the presence of siblings. Results were reported by the odds ratios (ORs) and 95% confidence interval (95% CI). The statistical tests were evaluated at the $p < 0.05$ significance level and constituted 2-tailed tests.

RESULTS

The general characteristics of the study subjects

The general characteristics of the study subjects were presented in **Table 1**. Of the total, 554 subjects (57.34%) were found to have one or more siblings. Slightly more than fifty percent of subjects were boys and 51.76% out of the total were 5–6 years old. About half of the total subjects fell into the underweight category based on the Kaup index. Single children had the highest tendency to have well-educated parents compared to children with siblings. Household income also showed a slightly higher correlation with single children than with. Single children tended to be more prone to FAs than ones with siblings. Households with only children tended to be nuclear families than stem families. In summation, it was found that the existence of siblings held a significant relationship with parents' education levels ($p < 0.001$), and household income ($p < 0.001$).

Supplementary Table 1 presented the general characteristics of children with/without FAs. It was found that 16.46% out of the total subjects had one or more FAs. Of children with FAs, 62.89% were allergic to only one food allergen. More than 30% of them were allergic to two or more allergens (data was not shown). The specific food items reported to cause FAs were shown in **Fig. 1**. Eggs appeared to cause FAs the most (all = 54, 4.69% for children with siblings vs. 6.79% for single children, $p < 0.05$). Shellfish followed next in order (2.71% for children with siblings vs. 5.58% for single children, $p < 0.05$). Single children were more likely to be caused FAs by fruits and milk and fish shrimp than children with siblings ($p < 0.05$), while

Table 1. General characteristics of the children with/without siblings

Variables	Subgroup	Total (n = 966)	Children with siblings (n = 554)	Single children (n = 412)	p-value
Age (years old)	3–4	466 (48.24)	258 (46.57)	208 (50.49)	0.23
	5–6	500 (51.76)	296 (53.43)	204 (49.51)	
Gender	Boys	501 (51.86)	278 (50.18)	223 (54.13)	0.22
	Girls	465 (48.14)	276 (49.82)	189 (45.87)	
Kaup index	Under weight	491 (50.83)	285 (51.44)	206 (50.00)	0.099
	Normal	353 (36.54)	190 (34.30)	163 (39.56)	
	Overweight	122 (12.63)	79 (14.26)	43 (10.44)	
Caregivers	Parents	816 (84.47)	467 (84.30)	349 (84.71)	0.98
	Grandparents	103 (10.66)	60 (10.83)	43 (10.44)	
	Maternal grandparents	47 (4.87)	27 (4.87)	20 (4.85)	
Education level of mother	Low	226 (23.40)	175 (31.59)	51 (12.38)	< 0.001*
	Medium	302 (31.26)	192 (34.66)	110 (26.70)	
	High	438 (45.34)	187 (33.75)	251 (60.92)	
Education level of father	Low	238 (24.64)	178 (32.13)	60 (14.56)	< 0.001*
	Medium	313 (32.40)	190 (34.30)	123 (29.85)	
	High	415 (42.96)	186 (33.57)	229 (55.58)	
Family structure	Nuclear family	492 (50.93)	305 (55.05)	187 (45.39)	0.006*
	Stem family	375 (38.82)	192 (34.66)	183 (44.42)	
	Others	99 (10.25)	57 (10.29)	42 (10.19)	
Household income	Low	199 (20.60)	140 (25.27)	59 (14.32)	< 0.001*
	Medium	374 (38.72)	222 (40.07)	152 (36.89)	
	High	393 (40.68)	192 (34.66)	201 (48.79)	

Note: Data are presented as number (%) for categorical measures. χ^2 test was used.
*$p < 0.05$.

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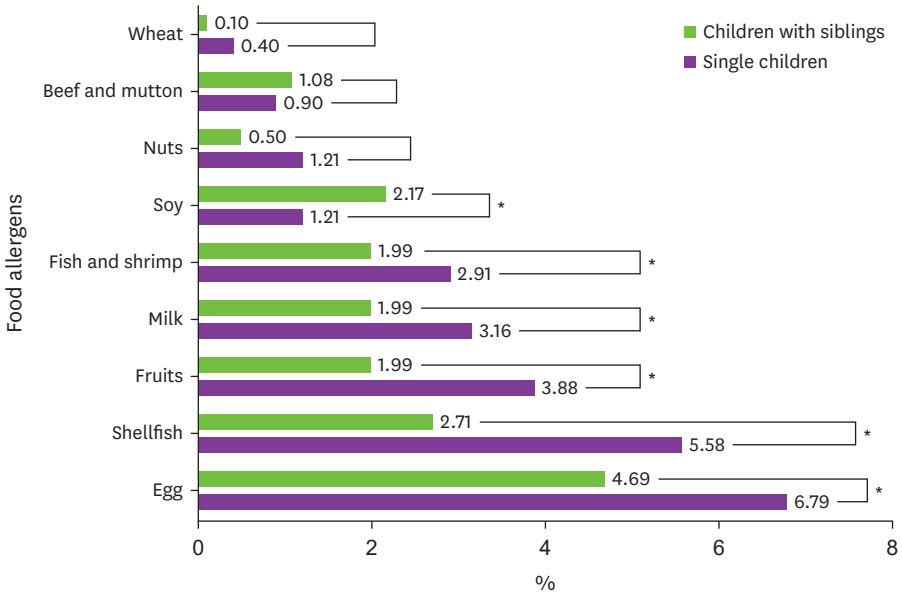

Fig. 1. The specific food items reported as causing food allergies by the study subjects.
Note: %, relative children with specific food allergies to all children by children with siblings and single children in this study. Nuts included peanuts and tree nuts and the item fruits included orange and mango. The χ^2 test was used.
*$p < 0.05$.

subjects with siblings tended to be more allergic to soy than single children (2.17% vs. 1.21%, $p < 0.05$). Among these nine items, wheat caused the least FAs.

The 5-underlying dimensions for the CSHQ scale

The EFA method suggested a 5-factor orthogonal solution (varimax rotation) for the underlying dimensions of CSHQ scale. Seven items did not remain in a factor due to their lower factor loading values than the cutoff threshold of 0.35. The 5 factors extracted through factor analysis consisted of 3 items to 10 items. Five factors were named as 'difficulty falling asleep', 'sleep anxiety', 'parasomnias', 'frequent night waking', and 'difficulty morning waking'. The 5 factors accounted for 63.78% of the variance with eigenvalues of 2.86, 2.13, 1.88, 1.78, and 1.49 in descending order. The factor loading values of consisting variables were presented in **Table 2**.

Association between food allergies and sleep problems

Table 3 displayed the total CSHQ score and scores for the 5 factors. Notably, 70.39% of the children had a total CSHQ score exceeding the clinical threshold for a sleep disorder. The 2-way ANCOVA method adopted to compare the total CSHQ scores and average factor scores for 'parasomnias', 'difficulty falling asleep', 'night waking', and 'sleep anxiety' showed no significant differences between children with siblings and single children, but scores for difficulty falling asleep were significantly higher in single children compared to those with siblings ($p = 0.03$). Notably, the single children indicated a higher prevalence of having FAs compared to the children with siblings ($p < 0.05$).

Table 4 showed the comparison of CSHQ scores between children with siblings and single children by additional classification of having FAs or not. For all children, the scores for 'difficulty falling asleep' and total CSHQ scores were found to be significantly higher when children had FAs ($p < 0.05$). Remarkably, factor scores of 'parasomnias' and 'sleep anxiety' were significantly higher when children had both siblings and FAs.

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Table 2. Final factor loadings of the CSHQ items (n = 966)

Items	Difficulty falling asleep	Sleep anxiety	Parasomnias	Frequent night waking	Difficulty morning waking
Item 1 – goes to bed at the same time	0.6542				
Item 2 – falls asleep in 20 min	0.3846				
Item 9 – sleeps too little	0.5265				
Item 10 – sleeps the right amount	0.7470				
Item 11 – sleeps the same amount each night	0.7181				
Item 4 – falls asleep in another's bed		0.4818			
Item 5 – needs parent in room to sleep		0.4345			
Item 6 – struggles at bedtime		0.4583			
Item 7 – afraid of sleeping in the dark		0.5259			
Item 12 – wets the bed at night			0.4164		
Item 13 – talks during sleep			0.4893		
Item 15 – sleepwalks			0.5500		
Item 16 – moves to another's bed in the night			0.4209		
Item 17 – grinds teeth during sleep			0.4199		
Item 18 – snores loudly			0.4673		
Item 19 – holds breath or stops breathing			0.4884		
Item 20 – snorts and gasps			0.5650		
Item 21 – trouble sleeping away			0.3730		
Item 22 – awakens screaming, sweating			0.5507		
Item 23 – alarmed by a scary dream				0.4638	
Item 24 – awakes once during the night				0.6796	
Item 25 – awakes more than once				0.7365	
Item 27 – wakes up in a negative mood					0.5691
Item 28 – others wake the child					0.4385
Item 29 – hard time getting out of bed					0.6546
Item 30 – takes a long time to be alert					0.5806
Eigen values	2.13	1.49	2.86	1.78	1.88
Variance explanation	8.91%	8.37%	30.79%	7.82%	7.89%

Note: Only loadings > 0.35 were presented. The other items were deleted in a factor due to their lower factor loading values than the cutoff threshold of 0.35.
CSHQ, Children's Sleep Habits Questionnaire.

Table 3. Comparison of sleep problem associated variables and food allergies between children with siblings and single children

Variables	Total (n = 966)	Children with siblings (n = 554)	Single children (n = 412)	p-value
Sleep problem				
Parasomnias	11.97 ± 2.16	11.89 ± 2.28	12.08 ± 1.99	0.49
Difficulty falling asleep	6.93 ± 1.70	6.91 ± 1.69	6.97 ± 1.71	0.24
Difficulty morning waking	5.98 ± 1.41	5.85 ± 1.33	6.14 ± 1.49	0.03*
Night waking	3.83 ± 1.11	3.80 ± 1.09	3.86 ± 1.13	0.33
Sleep anxiety	5.46 ± 1.20	5.52 ± 1.21	5.37 ± 1.18	0.08
Total score for CSHQ	44.46 ± 5.05	44.19 ± 5.06	44.84 ± 5.01	0.09
Sleep disorder (%)	680 (70.39%)	299 (72.57%)	381 (68.77%)	0.20
Food allergy				
One or more food allergies (%)	159 (16.46%)	74 (13.36%)	85 (20.63%)	0.03*

Note: Scores were presented as the means and standard deviation. Sleep disorder was evaluated as the CHSQ score higher than cut off score (cut-off score = 41). The analyses of covariance were used, with demographic factors (child's age, sex, parental education, family structure, and household income) as covariates. The χ^2 test was used to compare the percentage of sleep disorders and food allergies.
CSHQ, Children's Sleep Habits Questionnaire.
*p < 0.05.

Table 5 summarized the multiple logistic regression analyses to present the ORs for FAs according to the sleep problem-related variables for all subjects and additional separate analysis for children with siblings and single children, respectively. For all subjects, the 'difficulty falling asleep' factor and sleep disorder were significantly associated with increased OR of FAs. In brief, the OR of FAs increased with higher scores for 'difficulty falling asleep' (OR, 1.34; 95% CI, 1.22–1.48). And the odds of having FAs for children with sleep disorder was 2.35 times higher than children without sleep disorder (95% CI, 1.50–3.68), given all

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Table 4. Comparison of CSHQ scores with the additional classification of having FA or not by separate analyses of children with siblings and single children

Variables	Children with siblings (n = 554)			Single children (n = 412)		
	One or more FAs (n = 74)	No FA (n = 480)	p-value	One or more FAs (n = 85)	No FA (n = 327)	p-value
Parasomnias	12.43 ± 3.07	11.81 ± 2.13	< 0.001*	12.23 ± 1.89	12.03 ± 2.01	0.44
Difficulty falling asleep	7.71 ± 1.91	6.79 ± 1.63	< 0.001*	7.81 ± 1.99	6.76 ± 1.56	< 0.001*
Difficulty morning waking	5.91 ± 1.43	5.84 ± 1.32	0.6474	6.48 ± 1.63	6.05 ± 1.45	0.07
Night waking	3.78 ± 1.14	3.80 ± 1.09	0.7978	3.91 ± 1.13	3.85 ± 1.13	0.58
Sleep anxiety	5.81 ± 1.41	5.48 ± 1.17	0.0286*	5.55 ± 1.30	5.32 ± 1.15	0.09
Total score for CSHQ	46.21 ± 6.14	43.87 ± 4.81	< 0.001*	46.82 ± 5.59	44.32 ± 4.72	< 0.001*

Note: Scores were present as the means and standard deviation. The analyses of covariance were used, with demographic factors (child's age, sex, parental education, family structure, and household income) as covariates.
CSHQ, Children's Sleep Habits Questionnaire; FA, food allergy.
*p < 0.05.

Table 5. Odds ratios for food allergies according to CSHQ-associated variables in all children, children with siblings, and single children, separately

Variables	All subjects	Children with siblings	Single children
Parasomnias	1.08 (0.98–1.18)	1.14 (1.01–1.28)*	0.99 (0.87–1.46)
Difficulty falling asleep	1.34 (1.22–1.48)*	1.32 (1.14–1.52)*	1.38 (1.19–1.60)*
Difficulty morning waking	1.05 (0.92–1.19)	0.98 (0.80–1.19)	1.09 (0.91–1.31)
Night waking	0.91 (0.76–1.09)	0.82 (0.62–1.08)	0.98 (0.77–1.26)
Sleep anxiety	1.13 (0.97–1.32)	1.14 (0.91–1.42)	1.13 (0.90–1.40)
Sleep disorder			
No	1 (Ref.)	1 (Ref.)	1 (Ref.)
Yes	2.35 (1.50–3.68)*	2.48 (1.30–4.72)*	2.14 (1.13–4.06)*

Note: Data are presented as odds ratio (95% confidence interval) values using logistic regression analyses. Sleep disorder was evaluated as the CHSQ score higher than cut off score (cut-off score = 41). The logistic regression models were adjusted for the factor scores of parasomnias, difficulty falling asleep, difficulty morning waking, frequent night waking, and sleep anxiety, and some general variables including the presence of siblings, age, sex, Kaup index, family structure, father and mother education level, and household income.
CSHQ, Children's Sleep Habits Questionnaire.
*p < 0.05.

confounding variables remained controlled. But no significant effect of the factor scores for 'parasomnias', 'difficulty morning waking', 'frequent night waking', and 'sleep anxiety' on the OR of FAs were found. Subgroup analysis showed that the probability of FAs significantly increased with the 'difficulty falling asleep' (OR, 1.32; 95% CI, 1.14–1.52 vs. OR, 1.38; 95% CI, 1.19–1.60) and sleep disorder (OR, 2.48; 95% CI, 1.30–4.72 vs. OR, 2.14; 95% CI, 1.13–4.06) in all children, with and without siblings, respectively. The 'parasomnias' was positively associated only for children with siblings (OR, 1.14; 95% CI, 1.01–1.28).

DISCUSSION

As previous studies indicated that cases of FAs and sleep problems among Chinese preschool children have increased in recent years, we found that 16.46% of parents reported their children had experienced FAs in the past year, despite having no family history of allergies, no household pets, and not being born via cesarean section. This rate was higher than what was observed in preschool children in Wenzhou (12.86%) [30], an eastern city in China, but lower than the rate reported in Beijing (41.8%) [31]. A multi-city study conducted in China also reported a self-reported prevalence rate of 6.65% for FAs among preschool-aged children [32]. Notwithstanding, the reaction caused by FA might be exaggerated by parents due to their anxiety [33]. Therefore, it is important to pay attention to the high occurrence of FAs reported by parents of urban western preschool children, particularly when compared with parental reports from other countries such as Kuwait [34], Australia [35], and Thailand [33].

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Of children with FAs, 62.89% were allergic to only one food allergen. More than 30% of them were allergic to two or more allergens. Eggs appeared to cause FAs the most in this study, which is consistent with the findings of previous studies [36]. Egg allergy is one of the most common FAs in young children, which affected up to one-tenth of Australian infants and United States children (< 5 years) [36]. In addition, we found that shellfish followed the next in order, similar to the study's findings in Hongkong [37]. The reason for this result may be that Chongqing, being a mountainous city in southwest China, is far from the sea and the subjects in our study may have had less access to shellfish [38]. In this study, a disparity was indicated in terms of significant food allergens between children with siblings and single children identified. Future studies may need to more extensively investigate various food allergens reported by children's caregivers and associated covariates including family structure, household size, and overall dietary pattern.

The CSHQ is widely used in clinical settings to screen for sleep problems in children [27]. However, some studies have shown that the scale's reliability improves when certain items are omitted. For instance, Sneddon [39], proposed a four-factor solution (sleep initiation, sleep distress, transition to waking, and sleep duration) using only 24 of the original 33 items. Tan et al. [29], also found that deleting certain items improved the psychometric quality of the CSHQ for urban Chinese preschoolers, resulting in a four-factor structure with 28 items. In our study, which focused on Chinese-Western children aged 4–6, we obtained a 5-factor orthogonal solution (using varimax rotation) by deleting seven items with lower loading scores. In terms of content, the five underlying dimensions were named as 'parasomnias' (which includes snoring loudly, breathing or stopping breathing and related items), 'difficulty falling asleep', 'difficulty morning waking', 'frequent night waking', and 'sleep anxiety' (afraid of sleeping in the dark, struggles at bedtime and related items), respectively.

A meta-analysis study showed that the prevalence rates of sleep problems among children in mainland China range from 15.3% to 76.3% [22]. Nearly 70% of parents in our study reported their children might have had sleep disorders (scores of CSHQ were higher than 41). However, it was observed that poor sleep quality was significantly higher in West China compared to South China (47.4% vs. 30.4%) [22]. Considering these findings, the sleep quality of the study subjects in this study was revealed to be considerably poor. One reason can be inferred is that the study was conducted in the middle of the coronavirus disease 2019 (COVID-19) pandemic period. Since the World Health Organization (WHO) declaration of a global pandemic in March 2020, more than 756 million people worldwide have been infected by the severe acute respiratory syndrome coronavirus 2 virus, which has contributed to over 6.8 million deaths [40]. As the pandemic unfolded, researchers have demonstrated its serious effects on sleep [41]. Considering this turmoil, this may be explained by the fact that the children in this study are younger and under rapid physical and mental development, which could have led to unstable sleep habits and rhythms. Preschoolers' sleep may be greatly affected under the influence of COVID-19, thus possibly reflecting common issues of sleep quality in young childhood. In addition, this data was reported by parents, which may cause recall bias. Meanwhile, parents may be overly sensitive about their children's health, leading to the possibility of overestimating related symptoms.

Significant associations between the 'difficulty falling asleep' factor, sleep disorder, and FAs were found in our study. These results are consistent with previous studies that have investigated the links between sleep problems and allergic diseases in children [2,16]. Although the ORs were near 1, the previous studies showed a similar finding: FAs were

closely associated with sleep disorders [14]. Previous studies showed that sleep problems might slightly affect the changes of T cytokines, including interleukin (IL)-2, IL-4, and interferon-c, which affect immunity and inflammatory state [42]. Immune dysregulation and inflammation have been well-documented as typical hallmarks of allergic conditions [43]. It has been found that sleep disorders might reduce the number of T-cells and natural killer cells, monocyte function, and alter circulating concentrations of the cytokines [44,45]. Thus, like other allergic diseases, sleep disorders might also affect FAs by influencing immune action and inflammatory response.

China is moving to an aging population; the Chinese government has enacted a three-child policy [17], which could result in an increase in the number of multiple-child families. Compared with children with siblings, we found the prevalence of FAs among single children was higher. A study identified that the presence of older siblings is associated with increased gut microbial diversity and richness during early childhood based on the *hygiene hypothesis* [19]. The *hygiene hypothesis* that David Strachan proposed is that allergic diseases were prevented by infection in early childhood, transmitted by unhygienic contact with older siblings [46]. In recent years, the microbiota was considered the second major environmental factor likely to influence susceptibility to FAs, through modulation of the mucosal immune system [47]. We speculate that the association between single children and FA might exist as the insufficiently rich microbial flora [19].

We found that the OR for FAs with 'parasomnias' was only significantly higher in children with siblings, not in single children. These results might be driven by the likely situation of co-sleeping with siblings when children have siblings. Co-sleeping is associated with several sleep disturbances for children, including bedtime resistance and parasomnias [48]. Additionally, recent studies have shown that having siblings is positively correlated with a higher occurrence of conflicts among themselves. These conflicts have been found to be linked to shorter sleep durations and an increased number of sleep problems in children [20]. Given the confluence of factors involving sleep problems, FAs, and the presence of siblings obtained in this study, it seems plausible to surmise that sleep disturbances may contribute to the manifestation or exacerbation of FAs [49]. Addressing sleep problems may thus potentially mitigate one of the contributing factors in the development of FAs. While the difference is small, more research is needed in the future about the direct relationship between FAs and the existence of siblings.

Facing several limitations, the results should be interpreted with caution. First, the association does not entail that any cause-and-effect can be inferred based on the cross-sectional design; the issues of temporal sequencing/causality need to be considered and discussed. Poor sleep was also reported as one of the symptoms of a wide range of extra-intestinal manifestations associated with children with GI FAs [13]. We cannot ascertain whether FAs lead to poor sleep quality or whether poor sleep quality cause children's susceptibility to FAs. Although we have taken precautions by excluding children with a history of allergies, cesarean births, and pets in the home, some confounding effects might still exist. Secondly, the presence of FA was reported by parents, which might cause an inaccurate determination of FAs. Parents might exaggerate the reaction caused by FA due to extensive sensitivity towards their children [33]. If possible, a skin prick test (SPT), specific immunoglobulin E (IgE) measurement, trial elimination diets, and food challenges are necessary for future study. Third, the assessment of sleep problems was based on parent reports through questionnaires, which might result in recall bias. Although, it has

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been established that sleep information gathered from parents is likely to be reliable [50]. However, the use of objective measures, such as actigraphy or polysomnography, would provide more accurate data in future studies.

As one of the few exploratory studies on FAs and sleep quality in preschool children conducted in Western China, this study suggested that 'difficulty falling asleep' and sleep disorder were associated with FAs among preschoolers with and without siblings, and the association of 'parasomnias' with FAs differed with the presence of siblings. Based on the above results, further prospective studies are necessary to address the underlying dimensions and possible meditation effects of having siblings with sleep problems, which might be helpful for a multidisciplinary approach of constant interest to improve children's quality of sleep and FAs in West China.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1

General characteristics of the children with/without FAs

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