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High Concurrence of Nocturnal Enuresis and Associated Factors among South Chinese Children

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Abstract

Background: Nocturnal enuresis (NE) is not an uncommon disease in children, and the prevalence and clinical features have regional variations, but the relative data is scanty in southern China. The aim of this study is to establish the prevalence of NE and predictive factors in a large population of South Chinese children.

Methods: From December 2013 to July 2014, 15547 questionnaires were distributed to parents and children of 14 primary schools in Guangzhou and Zhongshan.

Results: Correctly completed response rate was 74.6%. Overall NE prevalence was 10.9% (1260/11599). NE was significantly more frequent in boys (P<0.001). Prevalence decreased progressively from 6–7 years (13.6%) to 12–14 years (7.6%). Most children with NE wetted after midnight (63.3%), and fewer than once per week (76.6%). Nearly 16.4% of children with NE suffered from constipation. Children with NE stopped using diapers at older ages than children without NE (P<0.001), and 6.6% were still using diapers. Sleep-disordered breathing (SDB) was reported in 36.9% of cases; main symptoms were mouth breathing (38.5%), snoring (34.3%), and restlessness (30.5%). Family history was present in 22.5% and urinary system disease history in 9.4% of cases. Only 20.5% had received treatment, 0.9% with enuresis alarms and 5.4% with drugs. Parental self-help strategies included fluid restriction (25.2%) and voiding (85.9%) before bed, while 36.9% lacked awareness of NE.

Conclusions: The occurrence of NE was still high among primary school in south China. The possible factors include over-using diapers, positive family history, complicated with SDB, constipation, male gender and younger age.

Keywords: Nocturnal enuresis; Children; Multicenter; South China

Introduction

Nocturnal enuresis (NE) is defined as intermittent incontinence of urine during sleep in children older than 5 years [1]. Primary nocturnal enuresis (PNE) is the condition when the symptom has existed always and the patient has not been dry for a period longer than 6 months, while secondary nocturnal enuresis (SNE) is the condition when there has been a symptom-free interval of 6 months. According to the presence of daytime lower urinary tract symptoms (LUTS) of bladder dysfunction, non-monosymptomatic nocturnal enuresis (NMNE) (LUTS present) and monosymptomatic nocturnal enuresis (MNE) (LUTS not present) are differentiated. Estimates of NE prevalence have ranged from 4.5% to 28.6% in different countries [2-9], likely reflecting variation in subject age, study inclusion criteria, genetic heterogeneity among populations, cultural factors, and educational levels. Generally lower incidences were reported in China, from 3.5% to 5.5% [6,10,11]. NE is more frequent in boys, with the male: female ratio varying from 1.4:1 to 2.9:1 across studies. The prevalence of NE decreases with age [2,13,14], indicating a high rate of spontaneous remission.

While NE is normally a benign developmental delay, it can be associated with more serious underlying conditions, including sleep disordered breathing (SDB) [15], possibly due to enhanced brain natriuretic peptide level [16]. Studies from other countries may not provide accurate predictions of NE prevalence and associated risk factors for children in southern China given regional variations in socioeconomic development, educational level, and other demographic and cultural factors. The aims of our study were to estimate the prevalence of NE among primary school-age children in Guangdong province

and to identify factors associated with NE, including possible underlying disorders.

Methods

A cross-sectional survey was conducted from December 2013 to July 2014 among parents of primary school students in Guangdong province. Using stratified and random cluster sampling methods, Guangzhou and Zhongshan were selected as the investigation areas. Eight schools in Guangzhou, 6 urban and 2 rural, and 6 in Zhongshan, 4 urban and 2 rural, were selected. All children in these 14 schools were eligible.

A total of 15547 self-administered questionnaires were distributed to the children and filled out by children and their parents. The questionnaire package also contained a consent form and a pamphlet with instructions for completing the questionnaire and background information on NE. Data collection in all schools was completed within one week. Written informed consent was obtained for all questionnaires used for data analysis. The study was approved by the ethics committee of the First Affiliated Hospital of Sun Yat-sen University. Written informed consent was obtained from parents or guardians of all children. The questionnaire consisted of three sections. The first section queried demographic information, such as age, gender, and grade. The second section queried NE-related data, including the time of wetting, frequency of NE, daytime symptoms, constipation, sleep quality, and the year that the child stopping using diapers. The frequency of NE was defined as follows: infrequent (less than once per week), moderately severe (2 - 5 wetting episodes per week) or severe (more than 6 wetting episodes per week). The third section contained items on past urinary and nervous system diseases, family history of NE, management strategies, treatments, and parental concerns about NE.

Returned questionnaires were checked and entered into a database. Some questionnaires were omitted due to missing information. Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS), version 20. Group differences in measurement data were evaluated by Student's t- tests and group differences in enumeration data by chi-squared tests. A logistic regression analysis was used to evaluate the association between risk factors and NE. P< 0.05 was considered statistically significant.

Results

A total of 11744 questionnaires were returned (total response rate of 75.5%), of which 145 were rejected due to the missing of important information, for a correct response rate of 74.6% (11599/11744). Mean age was 9.9 ± 1.9 years (range, 6–14 years), and male: female ratio was 1.2:1 (6300:5299). The overall prevalence of NE was 10.9% (1260/11599) and did not differ between study sites [11.6% (577/4984) in Guangzhou and 10.3% (683/6615) in Zhongshan; P>0.05]. There was a higher overall prevalence of NE among boys [12.2% (768/6300) vs. 9.3% (492/5299), P<0.001] but the difference was significant only in Zhongshan (12.1% vs. 8.0%, P<0.001; Guangzhou: 12.3% vs. 10.8%, P>0.05) **(Table 1)**.

Table 1 Overall prevalence of NE.

Gender	NE in Guangzhou		NE in Zhongshan		Total	
	n	%	n	%	n	%
Male	316	12.3	452	12.1	768	12.2
Female	261	10.8	231	8.0	492	9.3
Total	577	11.6	683	10.3	1260	10.9
χ2	2.813		29.337		25.096	
p-Value	0.101		<0.001		<0.001	

NE: nocturnal enuresis.

Overall, PNE was far more common than SNE (76.7% vs. 23.3%), and the ratio of PNE to SNE did not differ between males and females (P>0.05). The occurrence of MNE and NMNE was 90.2% and 9.8% respectively, and there is also no significant difference in MNE and NMNE between gender (P>0.05) **(Table 2)**.

Table 2 Prevalence of PNE, SNE, MNE and NMNE.

Gender	Children (n)	PNE (%)	SNE (%)	MNE (%)	NMNE (%)
Male	768	77.6	22.4	90.5	9.5
Female	492	75.4	24.6	89.8	10.2
Total	1260	76.7	23.3	90.2	9.8
p-Value		0.375		0.698	

PNE: Primary Nocturnal Enuresis; SNE: Secondary Nocturnal Enuresis; MNE: Monosymptomatic Nocturnal Enuresis; NMNE: Non-Mono-Symptomatic Nocturnal Enuresis.

Table 3 Prevalence of nocturnal enuresis by age.

Age (years)	Children (n)	Total (%)	Male (%)	Female (%)	χ2	p-Value
6–7	2116	13.6	14.9	12.2	3.150	0.076
8–9	3781	12.3	14.1	10.2	12.914	<0.001
10–11	3836	9.5	10.7	8.2	6.963	0.008
12–14	1866	7.6	8.9	5.9	5.714	0.017
Total	11599	10.9	12.2	9.3		

The majority of NE cases showed light to moderate wetting (wetting underwear only or wetting nightclothes), while only 20.6% (238/1156) exhibited heavy volume NE (wetting sheet). The commonest frequency of NE (76.6%) was fewer than once per week. Nearly 63.3% (733/1158) of NE cases wetted after

midnight. The overall prevalence of children with NE suffering from constipation was 16.4% **(Table 4)**.

Table 4 Frequency of incontinence symptoms by gender.

Items	Male		Female		Total		Gender predominance (p value)
	n	%	n	%	n	%	
Volume of wetting							
Light	413	57.6	252	57.4	665	57.5	0.719
Moderate	161	22.5	92	21.0	253	21.9	
Heavy	143	19.9	95	21.6	238	20.6	
Frequency of wetting							
Fewer than 1/wk	584	76.0	381	77.4	965	76.6	0.508
2-5/wk	133	17.3	74	15.0	207	16.4	
More than 6/wk	51	6.6	37	7.5	88	7.0	
Time of wetting							
< 2 h	79	11.1	59	13.3	138	11.9	0.026
2−4 h	159	22.3	128	28.8	287	24.8	
4−6 h	200	28.0	107	24.1	307	26.5	
> 6 h	276	38.5	150	33.8	426	36.8	
Constipation							
Yes	125	16.3	82	16.7	207	16.4	0.876
No	643	83.7	410	83.3	1053	83.6	

Of 4984 children with sufficient information on sleep behavior, SDB was reported in 36.9% (213/577) of NE cases compared to only 7.2% (318/4407) of children showing no NE (OR=7.5, P<0.001). Mouth breathing (38.5%, 82/213), snoring (34.3%, 73/213), and restless sleep (30.5%, 65/213) were the most common symptoms.

The ages at which children with NE stopped using diapers in daytime and nighttime (median, IQR) were both significantly older than in children without NE (daytime: 18.0, 12.0−25.0 vs. 14.0, 11.0−22.0 months; nighttime: 27.0, 20.0−36.0 vs. 24.0 17.0−30.0 months; both P<0.001), and 6.6% (83/1260) were still using diapers, the oldest child was at 13 years.

A substantially fraction of children with NE had a family history of NE [22.5% (283/1258)]. Histories of urinary and nervous system diseases were found in 9.4% (118/1260) and 1.5% (19/1260) of children with NE respectively.

Only 20.5% (258/1260) of children with NE had received treatments from their pediatricians, including 0.9% (11/1260) with enuresis alarms and 5.4% (68/1260) with drugs. Fluid restriction and voiding before bed were the most common parental self-help strategies [25.2% (318/1260) and 85.9% (1082/1260), respectively]. When parents were asked about attitudes toward their children with NE, 36.9% (420/1138) said 'It doesn't matter, and it will be OK when children grow up' **(Table 5)**.

Table 5 Parents attitude and treatment.

	n	%
Parents attitude		
Never mind	420	36.9
A little worry	621	54.6
Agonizing	97	8.5
Treatment		
Yes	258	20.5
No	1002	79.5
Behavioral strategy		
Fluid restriction	318	25.2
Voiding before bedtime	1082	85.9

A positive family history (odds ratio=12.804,P<0.001), SDB (odds ratio=7.524,P<0.001), constipation (odds ratio=2.719, P<0.001), male gender (odds ratio=1.356, P<0.001) and age (8-9, odds ratio=1.488,P<0.001;6-7,odds ratio=1.905,P<0.001) increased the probability of NE significantly. Logistic regression

analysis showed the association between risk factors and NE **(Table 6)**.

Table 6 Logistic regression analysis for risk factors.

Risk factors	NE (%)	Non-NE (%)	OR	95% CI	p-Value
Gender					
Female	9.3	90.7	1		
Male	12.2	87.8	1.356	1.204-1.529	<0.001
Age					
6-7	13.6	86.4	1.905	1.542 - 2.354	<0.001
8-9	12.3	87.7	1.488	1.262 - 1.754	<0.001
10-11	9.5	90.5	1.119	0.956 - 1.310	0.163
12-14	7.6	92.4	1		
Constipation					
No	9.8	90.2	1		
Yes	22.9	77.1	2.719	2.300-3.216	<0.001
Family history					
No	2.2	97.8	1		
Yes	22.5	77.5	12.804	8.550-19.172	<0.001
SDB					
No	8.2	91.8	1		
Yes	40.1	59.9	7.524	6.136-9.227	<0.001

Discussion

The NE prevalence found in this sample from southern China (10.9% among 6- to 14-year-old children) is lower than that reported in several developing countries, including Yemen (28.6% in children 6 to 15 years) and Congo (26.3%, 6–12 years) [3,17], but higher than in Hong Kong (4.6%, 6–11 years) [6], Taiwan (3.9%, 5–15 years) [11], and Henan province (4.1%, 5–18 years) [10]. A study from 8 Chinese cities reported a prevalence of 4.6% among 5- to 12-year-old children [18]. Thus, NE prevalence varies markedly among countries and regions within countries, reflecting socioeconomic differences, educational levels, heredity factors, and inclusion criteria. Consistent with most studies, overall prevalence was greater in boys [2,6,12,13,19], about a quarter of cases were SNE, and prevalence decreased with age. It is critical to identify underlying correlative secondary diseases, such as phimosis, urinary tract infection, spina bifida occulta (SBO), and psychological stressors. In this sample, a substantial minority of children with NE, more than one-third, also had SDB. Thus, NE is a sign of possible SDB, underscoring the importance of follow-up polysomnography (PSG) for chronic NE cases.

Possible factors contributing to NE include nocturnal polyuria, nocturnal detrusor over-activity, and high arousal thresholds [20]. In this study, 63.3% wetted after midnight, which may reflect the circadian rhythm of anti-diuretic hormone (ADH) and bladder filling in the second half of the night [21]. A study from Slovenia reported that 50.0% of children wetted more frequently after midnight, while only 15% wetted more frequently before midnight [13]. Our study showed that most children wetted fewer than once per week, which was similar to former studies [10,22].

Positive family history was found in 22.5% of NE cases, in accord with a study from northern China (21.2%) [10]. However, the influence of family history appears weaker in China than in several other countries, where 32.1% to 68.6% of children with NE have positive family histories [2,13,19,23]. Weintraub et al. also found that positive family history could markedly increase the risk for enuresis (OR 4.24) [12]. Thus, the NE genotype may differ markedly among ethnicities. Studies support a strong relationship between NE and several genes on chromosomes 8, 12, 13 and 22, although further studies are needed to identify the specific genes and the underlying etiologies [21,24-26].

In this sample, 9.8% of NE children also had daytime LUT symptoms. A larger proportion of older children (13–18 years) with NE showed combined daytime symptoms (21.2%) compared to younger NE cases [10], possibly reflecting increased prevalence of urinary tract infections and other bladder dysfunctions with age in children with NE. Therefore, NE with daytime symptoms may indicate underlying bladder

dysfunction, which can be resistant to conventional NE therapies.

Approximately 36.9% of NE cases had SDB, with mouth breathing, snoring, and restless sleep as typical symptoms. SDB can significantly increase the risk of NE (OR=7.524) and several previous studies also reported high rates of SDB in NE [4]. In one series, however, only 43.5% of NE cases were resolved after adenotonsillectomy [27]. Kovacevic et al. also found NE in 24% of children who underwent tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome, and almost of half of these NE cases did not resolve after surgery. The response to surgery was associated with presurgical NE severity, NMNE, obesity, positive family history of NE, and arousal difficulties [28]. Thus, NE appears strongly linked to SDB, but there were no significant differences in enuresis frequency in children with or without SDB with regard to frequency of enuresis. In any case, NE is an indication for further clinical study, including PSG, to detect possible underlying sleep disorders.

A preliminary study suggested that longer diaper use increases NE risk [10], but this is the first study to investigate the relationship between NE and diaper use quantitatively. Children with NE stopped using diapers at a significantly older age than children with NE. Prolonged diaper use may create reliance and ingrain the habit of urinating at any time, slowing training of the micturition reflex. In fact, the duration of diaper use may partly explain the variation in NE prevalence between countries.

It was reported that male gender, younger age, daytime incontinence, deeper sleep, positive family history of NE, attention deficit/hyperactivity disorder (ADHD), and constipation may also increase the NE risk [3,12,23], and our study indicated that a positive family history, SDB, constipation, male gender and age can significantly increase the NE risk.

Due to differences in education, income, and cultural practices, the frequency of medical consultation for NE varies greatly among countries, ranging from 6.1% to 36.0% [5,10,13,17,19]. In our study, only 20.5% of NE cases received professional treatments from pediatricians. Most parents relied on behavioral strategies, mainly restricting fluid and voiding before bedtime but with was little standardization of practices. More than one third of parents had limited awareness of NE and the association with potentially serious conditions such as SDB. Thus, it is important to improve awareness and correct misconceptions about NE to increase the frequency of professional treatment, especially when NE is a sign of a more serious underlying pathology.

Conclusion

Conclusively, the prevalence of NE among primary school students in south China was still high. Over-using diapers, positive family history, complicated with SDB, constipation, male gender and younger age may increase the possibility of NE. Most of children with NE were untreated, and awareness and perception of parents about NE need to be created.

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