



Verification for Diagnosis of Sleep-Related Hypoventilation and Carbon Dioxide Partial Pressure During Sleep in Children Using End-Tidal Carbon Dioxide

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Background and Objective From the past, several researchers have studied and measured the partial pressure of carbon dioxide during sleep in normal children to establish diagnostic criteria for hypoventilation in children. Here we tried to verify the existing definition of sleep-related hypoventilation in Asian by evaluating and analyzing the carbon dioxide partial pressure in pediatric subjects who underwent polysomnography.

Methods We retrospectively analyzed clinical information of 196 children who underwent polysomnography at our hospital from Feb 2011 to Apr 2021. Among Asian pediatric subjects, those with serious chronic or genetic diseases, craniofacial deformities, and hypoventilation confirmed by polysomnography were excluded. We evaluated partial pressure of carbon dioxide in target group by end-tidal carbon dioxide (EtCO₂) measured with a stream capnometer through nasal cannula. The target group was classified by apnea-hypopnea index and analyzed.

Results The mean value of the time with EtCO₂ ≥ 45 mm Hg in total sleep time was 47.00% which is higher than previous studies. The mean value of the time with EtCO₂ ≥ 50 mm Hg in total sleep time was 2.77% which is similar to previous studies. Also, our subjects showed the highest mean EtCO₂ value in non-rapid eye movement (NREM) stage and lowest mean EtCO₂ value when wake.

Conclusions In this study, the diagnostic criteria for sleep-related hypoventilation at the American Academy of Sleep Medicine (AASM) in 2017 established by measuring the EtCO₂ in western children seems appropriate to apply to Asian children to define hypoventilation.

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Keywords Sleep-related hypoventilation; End-tidal carbon dioxide; Sleep stages; Polysomnography; Carbon dioxide.

INTRODUCTION

Polysomnography (PSG) can be used to accurately diagnose pediatric sleep-disordered breathing, such as simple snoring, upper airway resistance syndrome, obstructive hypoventilation, sleep apnea, and sleep-related hypoventilation [1]. Sleep-related hypoventilation is a disorder in which the partial pressure of carbon dioxide (PCO₂) is increased due to problems with ventilation during sleep related to obesity, nervous system disease, or respiratory disease [2]. Conventional measurements of PCO₂ include arterial blood carbon dioxide

(PaCO₂), end-tidal carbon dioxide (EtCO₂) saturation, and transcutaneous carbon dioxide saturation (PtcCO₂). EtCO₂ is preferred for PSG, because it can be measured noninvasively and easily.

The diagnostic criteria for sleep-related hypoventilation in children is different from adult patients, owing to differences in the anatomical and physiological characteristics. For pediatric patients, the American Academy of Sleep Medicine (AASM) defines sleep-related hypoventilation as a prolonged state of PCO₂ ≥ 50 mm Hg lasting > 25% of the total sleep time (TST), as measured by PaCO₂, EtCO₂, or TcCO₂ [3]. Many researchers have investigated the measurements of PCO₂ during sleep in normal pediatric populations to establish diagnostic criteria for hypoventilation.

Montgomery-Downs et al. [4] performed PSG on a normal healthy pediatric population and reported the mean EtCO₂ value during TST as 40.7 mm Hg. The mean percentages of time for PCO₂ ≥ 45 mm Hg and PCO₂ ≥ 50 mm Hg out of TST were 21.6% and 2.8%, respectively. In a study by Uliel et al. [5], the mean percentages of time for PCO₂ ≥ 45 mm Hg and PCO₂ ≥ 50 mm Hg out of TST were 1.6% and 0.29%, respectively. Therefore, different studies have produced different measurement values. In contrast to previous studies, which used PaCO₂ more commonly than EtCO₂, recent PSG studies have tended to use EtCO₂ values, which may introduce differences. Nassar and Schmidt [6] reported that EtCO₂ measurements could be consistently lower than PaCO₂ measurements, indicating that EtCO₂ in PSG may produce different results than PaCO₂ as part of the diagnostic criteria. In addition, most prior studies defining hypoventilation during sleep have been conducted on Caucasian adults, while studies on Asian pediatric populations are rare. This study thus aimed to confirm PCO₂ values measured using EtCO₂ in pediatric subjects subjected to PSG. Measurements were analyzed to confirm the existing definition of sleep-related hypoventilation in the Asian pediatric population.

METHODS

The study protocol was approved by the Institutional Review Board of Ajou University Hospital (approval No. AJIRB-MED-MDB-22-168). This study was conducted at Ajou University Hospital from February 2011 to April 2021 on Asian pediatric participants aged 2 to 15 years old who underwent PSG for sleep disorder detection using EtCO₂ measurements. A total of 196 medical records were retrospectively analyzed after excluding those who were diagnosed with hypoventilation, or were found to have any significant chronic illness, genetic disease, or craniofacial deformity. EtCO₂ measurements were made using a side-stream capnometer (Capnostream[®]; Smiths Medical, Dublin, OH, USA) placed in a nasal cannula. The PSG (Embla N7000; ResMed, Amsterdam, Netherlands) consisted of six electroencephalography (EEG) channels (C3-A2, C4-A1, F3-A2, F4-A1, O1-A2, O2-A1), two electrooculography (EOG) channels, one electromyog-

raphy (EMG) channel, one electrocardiography (EKG) channel, and one pulse oximetry channel. An oronasal thermal sensor and nasal pressure transducer were also used to measure the airflow. A sleep expert interpreted all PSG measurements from the study participants following the AASM 2012. All statistical analyses were performed using R software (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was defined as a p-value < 0.05.

RESULTS

This study was conducted on a total of 196 children with a mean age of 6.00 ± 2.38 years (136 males [69.4%] and 60 females [30.6%]) (Table 1). The mean height, weight, and body mass index (BMI) of the children were 1.18 ± 0.16 m, 25.47 ± 14.39 kg, and 17.30 ± 4.10 kg/m² each. Additionally, the mean respiratory distress index (RDI) and sleep efficiency (SE) of the total patient group were 12.16 ± 23.66 and 0.90 ± 0.07, respectively.

The experimental group was classified based on the apnea-hypopnea index (AHI) as follows: 32, 98, 25, and 41 participants were assigned to the 0 ≤ AHI < 1, 1 ≤ AHI < 5, 5 ≤ AHI < 10, and 10 ≤ AHI groups, respectively (Table 2). For all subjects (n = 196), the mean value of the time (percentile fraction) with EtCO₂ ≥ 45 mm Hg in TST was 47.00% ± 33.79% (SD = 33.79, range = 0.00–99.36), while that with EtCO₂ ≥ 50 mm Hg was 2.77% ± 4.87% (SD = 4.87, range = 0.00–24.33).

In addition, the difference in the mean value of the time (percentile fraction) with EtCO₂ ≥ 45 mm Hg, that with EtCO₂ ≥ 50 mm Hg and the mean EtCO₂ of TST between each AHI groups were analyzed. There were no statistically significant differenc-

Table 1. Clinical characteristics of the total subjects related with polysomnography (n = 196)

Characteristic	Value
Age (yr)	6.00 ± 2.38
Sex	
Male	136 (69.4)
Female	60 (30.6)
Weight (kg)	25.47 ± 14.39
Height (m)	1.18 ± 0.16
BMI (kg/m ²)	17.30 ± 4.10
AHI	10.53 ± 23.48
RDI	12.16 ± 23.66
Neck (cm)	26.64 ± 3.76
Waist (cm)	57.61 ± 11.96
Hip (cm)	63.86 ± 11.56
Sleep efficiency	0.90 ± 0.07

Values are presented as mean ± standard deviation or n (%). BMI, body-mass index; AHI, apnea-hypopnea index; RDI, respiratory distress index.

Table 2. Mean value of time (percentile fraction) with EtCO₂ ≥ 45 mm Hg, EtCO₂ ≥ 50 mm Hg, mean EtCO₂ of TST (mm Hg) and differences between AHI groups

	p-value					Diff. (post-hoc p-value)*						
	0 ≤ AHI < 1 (n = 32)	1 ≤ AHI < 5 (n = 98)	5 ≤ AHI < 10 (n = 25)	10 ≤ AHI (n = 41)	Total (n = 196)	0 ≤ AHI < 1 1 ≤ AHI < 5	0 ≤ AHI < 1 5 ≤ AHI < 10	0 ≤ AHI < 1 10 ≤ AHI	0 ≤ AHI < 1 5 ≤ AHI < 10	0 ≤ AHI < 1 10 ≤ AHI	1 ≤ AHI < 5 10 ≤ AHI	5 ≤ AHI < 10 10 ≤ AHI
EtCO₂ ≥ 45 mm Hg												
Mean ± SD (%)	50.70 ± 37.31	51.22 ± 35.24	42.09 ± 30.34	37.03 ± 27.43	47.00 ± 33.79	-0.52	8.61	13.68	9.14	14.20	5.06	
Range (min-max, %)	0.12-99.36	0.00-99.09	0.00-77.67	0.00-82.75	0.00-99.36							
EtCO₂ ≥ 50 mm Hg												
Mean ± SD (%)	2.98 ± 5.20	2.38 ± 4.62	1.92 ± 4.35	4.05 ± 5.38	2.77 ± 4.87	0.61	1.06	-1.07	0.46	-1.68	-2.13	
Range (min-max, %)	0.00-22.46	0.00-21.40	0.00-20.80	0.00-24.33	0.00-24.33							
Mean EtCO₂ (average of W, NREM, REM)												
Mean ± SD (%)	44.39 ± 2.57	44.11 ± 2.86	43.06 ± 2.93	41.86 ± 5.34	43.54 ± 3.63	0.00	1.33 (0.55)	2.53 (0.02)	1.05 (0.61)	2.25 (0.01)	1.20 (0.59)	
Range (min-max, %)	39.70-49.30	33.60-52.20	34.07-46.40	25.70-55.07	25.70-55.07							

*Post-hoc: Tukey test. EtCO₂, end-tidal carbon dioxide; TST, total sleep time; AHI, apnea-hypopnea index; SD, standard deviation; W, wake stage; NREM, non-rapid eye movement; REM, rapid eye movement.

es in mean value of the time (percentile fraction) with EtCO₂ ≥ 45 mm Hg and that with EtCO₂ ≥ 50 mm Hg between each AHI groups. Likewise, there were no statistically significant differences in the mean EtCO₂ of TST between each AHI groups except for between 0 ≤ AHI < 1 group and 10 ≤ AHI group, 1 ≤ AHI < 5 group and 10 ≤ AHI group.

The mean EtCO₂ values in each sleep stage in all subjects and the groups with 0 ≤ AHI < 1 (n = 32), 1 ≤ AHI < 5 (n = 98), 5 ≤ AHI < 10 (n = 25), and 10 ≤ AHI (n = 41) were analyzed (Table 3). For all subjects, the mean EtCO₂ values in the wake, non-rapid eye movement (NREM) stage, and rapid eye movement (REM) stage were 41.94 mm Hg, 45.19 mm Hg, and 43.52 mm Hg each. In addition, the difference between the average EtCO₂ values of each stage was significant, as shown in the table (Wake-NREM = -3.25, p-value < 0.001; Wake-REM = -1.57, p-value = 0.001; NREM-REM = 1.68, p-value < 0.001). It showed the highest mean EtCO₂ value in non-REM sleep and lowest mean EtCO₂ value in the wake stage.

As in the previous analysis of the entire pediatric group, the pattern of increase and decrease in the mean EtCO₂ value in all four groups classified based on AHI showed the highest value in the non-REM stage and the lowest value in the wake stage.

Specifically, in the group with 0 ≤ AHI < 1, the mean EtCO₂ value for each sleep stage was 43.04 mm Hg in the wake stage, 46.02 mm Hg in the non-REM stage, and 43.88 mm Hg in the REM stage. In the subject group 1 ≤ AHI < 5, the mean EtCO₂ value for each sleep stage was 42.14 mm Hg in the wake stage, 46.18 mm Hg in the non-REM stage, and 44.04 mm Hg in the REM stage. For the group with 5 ≤ AHI < 10, mean EtCO₂ value for each sleep stage was 41.46 mm Hg in the wake stage, 44.51 mm Hg in the non-REM stage, and 43.15 mm Hg in the REM stage. In the group with 10 ≤ AHI, the mean EtCO₂ value for each sleep stage was 40.90 mm Hg in the wake stage, 42.62 mm Hg in the non-REM stage, and 42.25 mm Hg in the REM stage.

The difference between the mean EtCO₂ values of each stage in the entire pediatric group and the four target groups classified based on AHI was statistically significant, as shown in the table, except for the differences in mean EtCO₂ values between the wake and REM stages in the 0 ≤ AHI < 1 group, between the wake and REM stages in the 5 ≤ AHI < 10 group, between the NREM and REM stages in the 5 ≤ AHI < 10 group, and between any of the sleep stages in the 10 ≤ AHI group.

In this study, the patterns of mean, highest, and lowest EtCO₂ for each sleep stage based on the mean oxygen saturation during the TST in the entire pediatric population were evaluated (saturation of percutaneous oxygen [SpO₂] > 95% vs. SpO₂ < 95%) (Table 4). The mean EtCO₂ values of the subjects with mean oxygen saturation over 95% during total sleep were 42.07 mm Hg, 45.41 mm Hg, and 43.57 mm Hg for the wake, NREM, and REM stages, respectively, and the overall average value was 43.69 mm Hg. Mean EtCO₂ values of the subjects with mean oxygen saturation below 95% during total sleep were 39.85 mm Hg, 41.55

Table 3. Mean EtCO₂ level during sleep stage classified by AHI in all subjects (n = 196)

	W	NREM	REM	Total	W-NREM		W-REM		NREM-REM	
					Diff.	p-value	Diff.	p-value	Diff.	p-value
ALL (n = 196)	41.94 ± 4.66	45.19 ± 4.12	43.52 ± 4.06	43.55 ± 4.50	-3.25	< 0.001	-1.57	< 0.001	1.68	< 0.001
0 ≤ AHI < 1 (n = 32)	43.04 ± 3.67	46.02 ± 3.31	43.88 ± 3.11	44.32 ± 3.58	-2.97	< 0.001	-0.84	0.97	2.13	0.02
1 ≤ AHI < 5 (n = 98)	42.14 ± 4.89	46.18 ± 2.84	44.04 ± 3.01	44.12 ± 4.07	-4.04	< 0.001	-1.90	< 0.001	2.14	< 0.001
5 ≤ AHI < 10 (n = 25)	41.46 ± 2.72	44.51 ± 3.22	43.15 ± 4.41	43.04 ± 3.65	-3.05	< 0.001	-1.68	0.36	1.36	0.68
10 ≤ AHI (n = 41)	40.90 ± 5.57	42.62 ± 6.22	42.25 ± 5.96	41.92 ± 5.92	-1.72	0.55	-1.34	0.87	0.38	> 0.999

Values are presented as mean ± standard deviation unless otherwise indicated.

EtCO₂, end-tidal carbon dioxide; AHI, apnea-hypopnea index; W, wake stage; NREM, non-rapid eye movement; REM, rapid eye movement.

Table 4. Mean EtCO₂ level during sleep stage classified by O₂ saturation level in all subjects (n = 196)

SpO ₂	W	NREM	REM	Total
Mean ± SD (mm Hg)				
Over 95% (n = 185)	42.07 ± 4.28	45.41 ± 3.75	43.57 ± 3.81	43.69 ± 4.19
Below 95% (n = 11)	39.85 ± 9.07	41.55 ± 7.56	42.64 ± 7.10	41.34 ± 7.79
Highest ± SD (mm Hg)				
Over 95% (n = 185)	50.99 ± 3.03	51.92 ± 2.52	49.88 ± 3.44	50.95 ± 3.12
Below 95% (n = 11)	52.07 ± 4.90	55.03 ± 5.85	100.75 ± 153.70	69.28 ± 88.95
Lowest ± SD (mm Hg)				
Over 95% (n = 185)	22.38 ± 8.92	21.88 ± 10.33	28.77 ± 9.60	24.23 ± 10.10
Below 95% (n = 11)	22.40 ± 12.92	16.06 ± 8.27	17.34 ± 8.08	18.60 ± 10.09

Values were described by mean EtCO₂ level with SD.

EtCO₂, end-tidal carbon dioxide; SpO₂, saturation of percutaneous oxygen; SD, standard deviation; W, wake stage; NREM, non-rapid eye movement; REM, rapid eye movement.

mm Hg, and 42.64 mm Hg for the wake, NREM, and REM stages, respectively, and the overall average value was 41.34 mm Hg.

In all sleep stages, the mean EtCO₂ values of the subjects with mean oxygen saturation below 95% were lower than those of the subjects with mean oxygen saturation over 95%, without statistical significance.

Additionally, this study analyzed the relationship between AHI, apnea, hypopnea, mean, highest, and lowest EtCO₂, and mean oxygen saturation in all pediatric subjects (Table 5). We found that the mean EtCO₂ decreased by 0.02 per unit increment in AHI, which was a statistically significant result. The mean EtCO₂ decreased by 0.03 per unit increase in apnea and hypopnea; however, this was not significant.

The highest EtCO₂ tended to increase significantly with AHI, apnea, and hypopnea, as shown in the Table 5. In contrast, the lowest EtCO₂ showed a decreasing pattern when AHI, apnea, and hypopnea increased, and this difference was statistically significant. Finally, mean oxygen saturation showed a slight decreasing pattern when AHI, apnea, and hypopnea increased, which was statistically significant (measured values of -0.00049, -0.00072, and -0.00082, respectively).

DISCUSSION

In contrast to waking time, hypoventilation can occur easily during sleep because tidal volume, respiratory rate, and ventilatory drive tend to decrease. From waking to sleep, the PCO₂ may increase by 2–8 mm Hg, the partial pressure of oxygen (PO₂) may decrease by 3–10 mm Hg, and SpO₂ may decrease by 2% [2,7,8]. In adults, sleep-related hypoventilation can be accompanied by myasthenia gravis and amyotrophic lateral sclerosis, or may manifest as obesity hypoventilation syndrome or congenital central hypoventilation syndrome, accompanied by hypothalamic dysfunction [9]. Obstructive hypoventilation is more common in pediatric patients than in adults because, apart from obstructive sleep apnea or hypopnea, ventilatory disorders can occur due to persistent partial obstruction of the upper airway [10]. Pediatric sleep-related hypoventilation can also be observed in excessive obesity, apart from congenital central hypoventilation syndrome, Down syndrome, and neuromuscular diseases, which is similar to the situation observed in adults [11,12]. Many researchers have measured and analyzed PaCO₂ to establish the diagnostic criteria for sleep during hypoventilation. However, most studies have been conducted on Caucasian populations, and the results may not be generalizable to Asian populations. Numerous studies have reported differences in respiratory physiology and sleep states between different ethnic groups. Accord-

Table 5. Relationship between AHI, apnea, hypopnea and mean/highest/lowest EtCO₂/mean oxygen saturation level in all subjects (n = 196)

	Estimate	Std. error	t value	p-value
Mean EtCO ₂				
AHI	-0.02	0.01	-2.11	0.04
Apnea index	-0.03	0.02	-1.78	0.08
Hypopnea index	-0.03	0.02	-1.84	0.07
Highest EtCO ₂				
AHI	0.29	0.03	8.77	< 0.001
Apnea index	0.64	0.05	12.78	< 0.001
Hypopnea index	0.23	0.07	3.47	< 0.001
Lowest EtCO ₂				
AHI	-0.09	0.02	-4.34	< 0.001
Apnea index	-0.12	0.04	-3.24	< 0.001
Hypopnea index	-0.16	0.04	-4.17	< 0.001
Mean oxygen saturation				
AHI	0.00	0.00	-20.99	< 0.001
Apnea index	0.00	0.00	-15.44	< 0.001
Hypopnea index	0.00	0.00	-15.14	< 0.001

AHI, apnea-hypopnea index; EtCO₂, end-tidal carbon dioxide.

ing to Peterson et al. [13], the diurnal cortisol slope in African Americans is less steep than that in Caucasian Americans, which is partly attributable to disparate night sleep times between the two ethnic groups. Kumari et al. [14] reported a correlation between short sleep duration and a flat diurnal cortisol slope on the day after sleep. Based on this finding, it can be postulated that sleep characteristics are influenced by ethnic differences in cortisol levels and the hypothalamic-pituitary-adrenal axis. Additionally, Borker et al. [15] reported that a short hypopnea–apnea duration in the NREM sleep stage is associated with younger age, female sex, and black ethnicity. The authors also reported that hypopnea–apnea duration is significantly longer in Asians. Marcus et al. [16] reported that for normal Caucasian pediatric subjects, the EtCO₂ increased by 4–10 mm Hg during the sleep state compared to the awake state, and the measurement values were lower during REM sleep than those for NREM sleep. Moreover, Sonnappa et al. [17] studied normal healthy Asian and Caucasian pediatric subjects, and their results indicated a significant difference between the two ethnic groups in terms of fractional exhaled nitric oxide and forced expiratory capacity of the lungs. The authors concluded that ethnic differences should be considered for effective breathing control during both the awake and sleep states in pediatric patients. Currently, there is a lack of studies on pediatric Asian populations; as such, more studies are needed in this group, as results from studies in adults or other ethnicities are weakly generalizable.

For all participants (n = 196) in the 0 ≤ AHI < 1 group (n = 32), 1 ≤ AHI < 5 group (n = 98), 5 ≤ AHI < 10 group (n = 25),

and 10 ≤ AHI group (n = 41), the mean value of time with EtCO₂ ≥ 45 mm Hg and that with EtCO₂ ≥ 50 mm Hg was calculated. A previous study by Montgomery-Downs et al. [4] was conducted on normal pediatric subjects after excluding those who snored, those with an AHI ≥ 1, and those with other diseases. The authors reported that the mean TST with EtCO₂ ≥ 45 mm Hg and EtCO₂ ≥ 50 mm Hg were 21.6% and 2.8%, respectively. Compared with the above results, the results from this study showed significantly higher values of the mean value of time with EtCO₂ ≥ 45 mm Hg. The difference between the two studies may have stemmed from the age difference of the study subjects: 3.2–8.6 years in Montgomery-Downs et al. [4] vs. 2–15 years in our study. Additionally, our study did not exclude those who snored or had an AHI ≥ 1. The mean BMI of the participants in our study was 17.2 kg/m², which also differed from those in Montgomery-Downs et al. [4], which were 16.7 (3–5 years) and 17.1 (6–7 years). In addition to the aforementioned factors that might have contributed to the difference, this study was conducted on an Asian ethnic group, explaining the difference in the mean value of time with EtCO₂ ≥ 45 mm Hg. The mean time with EtCO₂ ≥ 50 mm Hg in our study did not differ significantly from that of Montgomery-Downs et al. [4]; thus, this study supports the existing diagnostic criteria for sleep-related hypoventilation by the AASM.

Also, the difference in the mean value of the time (percentile fraction) with EtCO₂ ≥ 45 mm Hg, that with EtCO₂ ≥ 50 mm Hg and the mean EtCO₂ of TST between each AHI groups were calculated in this study. We identified statistically significant differences in the mean EtCO₂ of TST between 0 ≤ AHI < 1 group and 10 ≤ AHI group, 1 ≤ AHI < 5 group and 10 ≤ AHI group. This differences between the groups may be considered as a result of increased apnea and hypopnea event in the group with high AHI.

Moreover, this study analyzed the mean EtCO₂, highest EtCO₂, and lowest EtCO₂ for all sleep stages in all participants. The mean EtCO₂ values during the wake, NREM, and REM stages were 41.94 mm Hg, 45.19 mm Hg, and 43.52 mm Hg, respectively. The differences in the mean EtCO₂ between the stages were significant. The maximum mean EtCO₂ and minimum mean EtCO₂ were found during the NREM and wake stages.

Additionally, this study investigated the changes in EtCO₂ for individual sleep stages in the 0 ≤ AHI < 1 (n = 32), 1 ≤ AHI < 5 (n = 98), 5 ≤ AHI < 10 (n = 25), and 10 ≤ AHI (n = 41) groups. Similar to the whole group analysis results, all four groups showed the maximum mean EtCO₂ during the NREM stage and the minimum mean EtCO₂ during the wake stage. Previous studies have generally excluded those with AHI ≥ 1, whereas this study classified the participants into different groups based on AHI. Each group was analyzed for EtCO₂ trends during different sleep stages.

We confirmed EtCO₂ measurements during each sleep stage using SpO₂ as a reference in all groups. The mean EtCO₂ value of the group with < 95% SpO₂ during sleep was lower than that of the group with ≥ 95% SpO₂ at all sleep stages. Those with <

95% SpO₂ may have had significantly more frequent apnea events when capnography could not provide meaningful measurements, leading to a low mean EtCO₂ value.

Finally, this study analyzed the relationship between AHI, apnea, hypopnea, and the mean, highest, and lowest EtCO₂ levels in all pediatric subjects. We found that the mean EtCO₂ significantly decreased by 0.02 per unit increment in AHI. This could be considered as a compensatory effect due to the increase in the highest EtCO₂ value and the decrease in the lowest EtCO₂ value as the AHI increases.

EtCO₂ and PtcCO₂ are noninvasive methods for measuring PaCO₂ during sleep [18]. EtCO₂ was measured from the air outflowing from the nasal cannula via capnography. The alveoli gas is diluted by mixing with the gas in the airway and atmospheric air, meaning that EtCO₂ cannot be the same as PaCO₂. Moreover, EtCO₂ is considered unreliable when the subject is breathing through the mouth, or when there is no airflow through the nasal cannula owing to apnea [19,20]. According to Morielli et al. [21], EtCO₂ measurement is significantly different from PtcCO₂ measurement in pediatric patients. Thus, both methods are recommended for estimating PaCO₂.

In this study, we calculated the mean value of time with EtCO₂ ≥ 45 mm Hg, as well as with EtCO₂ ≥ 50 mm Hg to verify the definition of hypoventilation. A limitation of this study is that we did not exclude subjects with AHI ≥ 1 or those who snored.

Of the values obtained for all pediatric subjects, the mean value of time with EtCO₂ ≥ 45 mm Hg was 47.00% ± 33.79% (SD = 33.79, range = 0.00–99.36) and that with EtCO₂ ≥ 50 mm Hg was 2.77% ± 4.87% (SD = 4.87, range = 0.00–24.33). Compared with previous studies, the mean time with EtCO₂ ≥ 45 mm Hg in this study was larger. Montgomery-Downs et al. [4] reported that the mean values of time with EtCO₂ ≥ 45 mm Hg and that with EtCO₂ ≥ 50 mm Hg were 21.6% and 2.8%, respectively. Uliel et al. [5] and Gozal et al. [22] reported that the mean time with EtCO₂ ≥ 45 mm Hg were 1.6% and 2.0%, respectively. Thus, the measurement values varied in previous studies. Of note, Uliel et al. [5] regarded values occurring when PCO₂ ≥ 50 mm Hg or when PCO₂ ≥ 45 mm Hg exceeded 10% of the TST as outliers.

This study measured the mean time with EtCO₂ ≥ 45 mm Hg and EtCO₂ ≥ 50 mm Hg. The overall findings of our study are consistent with those of previous studies. The mean EtCO₂ level for each sleep stage (wake, NREM, and REM) was measured in pediatric patients, revealing that the mean EtCO₂ had a minimum in the wake stage and a maximum in the NREM stage. Additionally, the EtCO₂ of the group with SpO₂ < 95% was lower than that of the group with ≥ 95% SpO₂ during sleep.

The current criteria for diagnosing sleep-related hypoventilation, established by the AASM in 2017, involves measuring and analyzing EtCO₂ saturation. Based on the results of this study, we believe that although the existing criteria were developed for Caucasian pediatrics, they can be applied to Asian pediatric individuals.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Author Contributions

Conceptualization: Hyun Jun Kim. Data curation: Jang Gyu Han, Hannah Park, Ji Sun Yang. Formal analysis: Jang Gyu Han, Hyun Jun Kim. Funding acquisition: Hyun Jun Kim. Investigation: Jang Gyu Han. Methodology: Hyun Jun Kim. Project administration: Hyun Jun Kim. Resources: Hyun Jun Kim. Software: Ji Su Kim, Bumhee Park. Supervision: Hyun Jun Kim, Do-Yang Park. Validation: Hyun Jun Kim. Visualization: Jang Gyu Han, Hannah Park, Ji Sun Yang. Writing—original draft: Jang Gyu Han. Writing—review & editing: Hyun Jun Kim, Do-Yang Park.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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