Characteristics of sleep-disordered breathing in children with down syndrome - A comparison with typically developing children

Hiroyuki Sawatari a,1, Anita Rahmawati b,1, Nobuko Moriyama c, Kanae Fujita c, Tomoko Ohkusa d, Tomoko Nao d, Nobuko Hashiguchi c, Mari Nishizaka e, Shin-ichi Ando f, Akiko Chishaki g,*

a Department of Perioperative and Critical Care Management, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan b Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia c Department of Health Sciences, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan d Faculty of Health Sciences, Department of Nursing, Ube Frontier University, Yamaguchi, Japan e Kirameki Project Carrier Support Center, Kyushu University Hospital, Fukuoka, Japan f Sleep Apnea Center, Kyushu University Hospital, Fukuoka, Japan g Fukuoka Dental College Hospital and Fukuoka Nursing College, Graduate School of Nursing, Fukuoka, Japan

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ABSTRACT

Background: Compared with typically developing control children (CC), children with Down syndrome (DS) frequently exhibit sleep-disordered breathing (SDB) and unusual sleep postures (USPs). No studies have directly compared SDB-related signs and symptoms, SDB-related parameters, and USPs between children with DS and CC. This study aimed to evaluate the prevalences of SDB and USPs in children with DS and CC.

Methods: We analyzed SDB-related parameters measured via overnight pulse oximetry and questionnaires administered to parents on SDB-related signs and symptoms, including sleeping postures. Estimated SDB was defined as a 3% oxygen desaturation index (ODI) ≥5 dips/h.

Results: Fifty-one children with DS (4–5 years: N = 12, 6–10 years: N = 23, 11–15 years: N = 16) and sixty-three CC (4–5 years: N = 18, 6–10 years: N = 27, 11–15 years: N = 18) were included. The prevalence of estimated SDB and observed USPs was higher in children with DS than in CC (p < 0.0001). Among children aged 11–15 years old, but not those aged 4–5 and 6–10 years old, frequency of arousal and apnea (p = 0.045 and p = 0.01, respectively) were higher in children with DS than in CC. Multivariate analyses showed that DS was associated with SDB-related signs and symptoms, estimated SDB, 3% ODI, average oxygen saturation (SpO2), and nadir SpO2, while USPs were associated only with higher values of SpO2 <90%.

Conclusions: Estimated SDB tended to increase in children with DS but decreased in CC with growth. USPs were more frequent in children with DS than in CC, especially in older children. USPs might indicate severe hypoxemia due to SDB in DS.

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1. Introduction

Down syndrome (DS) is a common inherited chromosomal disorder, which is estimated to occur in 1/650 to 1/1000 live births [1,2]. Children with DS are at an increased risk of developing sleep-disordered breathing (SDB) than typically developing children [3,4]. SDB in DS results mainly from hypotonia, macroglossia, and midface hypoplasia [5]. Progressive obesity is another risk factor in adolescents with DS [6]. Children with DS also have an increased risk for congenital heart disease (CHD) and pulmonary hypertension, which are potentially associated with disrupted sleep [6,7]. Since the presence of SDB in children could be a risk factor for attention difficulty, disturbance of normal intellectual development, and exacerbation of cardiovascular diseases, early detection...
and treatment of SDB should be mandatory in children, even those without DS [8,9].

The American Academy of Pediatrics recommends a sleep study to screen for SDB in children with DS, even at early ages. However, a sleep study using type-I polysomnography (PSG) has several disadvantages, including its high cost and the difficulty in performing the test with many sensors, especially in children with DS who also have intellectual disability [10,11]. Initial screening with pulse oximetry could be an alternative tool for cases in which a diagnostic multichannel PSG study is difficult to perform, and it might provide patients early access to essential therapy for SDB [12,13].

A previous study reported that unusual sleep postures (USPs), such as sitting and leaning forward, were frequently observed in patients with DS [14]. Positional therapies are known to be effective in obstructive sleep apnea (OSA) [15]. If the USPs in children were self-defending behaviors to prevent airway collapse during sleep, then these could be considered supportive signs for the existence of SDB. Since parent-child co-sleeping is common in Asian countries, we hypothesized that we could collect reliable data from parents regarding their children’s sleep characteristics or postures that might help in the early detection of SDB [16].

Accordingly, the objectives of the current case–control study were as follows: 1) to assess the differences in SDB-related parameters and SDB-related signs and symptoms, including USPs, between children with DS and typically developing control children (CC) in different age groups, and 2) to examine the relationships between SDB-related parameters and USPs in children with DS and CC.

2. Methods

2.1. Participants

We recruited children with DS who were members of the Japan Down Syndrome Society in Yamaguchi and Fukuoka Prefectures. An explanatory letter, questionnaires, and a pulse oximeter were sent via post. After completing the questionnaire and overnight pulse oximetry measurements, the parents returned them to the researchers in prepaid envelopes. Children without DS (ie, CC) who had no underlying diseases were randomly selected from several elementary and junior high schools in the same prefectures as the children with DS, and these included the siblings of children with DS. This research was conducted between 2015 and 2018, with the understanding and written informed consent of each participant and their parents. The study was approved by the Ethics Committee of Kyushu University Graduate School of Medical Sciences and Ube Frontier University. The study procedures followed were in accordance with the Declaration of Helsinki.

2.2. Overnight pulse oximetry

Children with DS and CC underwent overnight pulse oximetry measurements (PULSOX-Me300, Konica Minolta Sensing, Inc., Tokyo, Japan) for 2 or 3 consecutive nights at home. In addition to providing the parents written instructions and illustrations about performing overnight pulse oximetry measurements, a mini-seminar was held to explain the use of the device. A pulse oximeter was attached to the study participants before sleeping at home. To avoid the first-night effect, the recording results from the first night were discarded. We used the 3% oxygen desaturation index (ODI), representing the number of ≥3 desaturation events per hour of recording time, as a marker for the frequency of hypoxemia. The criteria for SDB in children for evaluating the presence of SDB are still under debate [4]. We set the cutoff value for the definition of SDB as 3% ODI ≥5 dips/h, which is same definition as that in adults. The average arterial oxygen saturation level (average SpO₂), ratio of arterial oxygen saturation less than 90% (SpO₂ <90%), and nadir values of arterial oxygen saturation levels (nadir SpO₂) were also used. All recorded data were manually double-checked by a certified sleep technician and a medical doctor, both of whom were blinded to the participants’ characteristics, to adopt only artifact-free recording periods, using a data analysis software (DS-Me version 2.10; Minolta, Tokyo, Japan).

2.3. Questionnaires

The parents completed a questionnaire on age, sex, body weight, body height, presence of CHD, and SDB-related signs and symptoms, such as witnessed midnight arousal, snoring, apnea, and daytime sleepiness [17,18]. The Japanese version of the Epworth Sleepiness Scale (ESS) was also answered by the parents, and a higher ESS value indicated that the person had more severe daytime sleepiness [19,20]. Witnessed apnea was defined as a complete pause of breathing followed by restarting of breathing with rapid gasping for air [10]. The questionnaire for SDB-related signs and symptoms was answered by selecting one of the four following choices: “Frequently” (5−7 nights/week), “Sometimes” (1−4 nights/week), “Never” (0 night/week), or “Unknown.” When the parents answered a question as “Frequently” or “Sometimes,” we regarded the answers as “positive” or “yes.” We also regarded the data as “Missing” when the parents answered a question as “Unknown,” and thus, the denominator of each variable for calculating the percentage was different from the others. Because parent-child co-sleeping is common, especially in children with comorbid conditions in Japan, habitual sleep postures and subjective sleeping time are evaluated on the basis of parental observation [16]. Sleep postures were categorized as usual (supine and lateral), prone, and unusual (leaning forward with legs backward, leaning forward with legs forward, leaning forward with legs crossed, and sitting) (Fig. 1). Sleep postures were classified as usual postures in the absence of unusual or prone postures. USPs were defined as the presence of one or more sitting or leaning forward postures (legs backward, forward, or crossed), and a prone posture was defined as a prone posture without USPs [10]. The subjective sleeping time was estimated as the sleeping time based on data from the questionnaires for overnight pulse oximetry measurements.

2.4. Statistical analysis

STATA version 15.1 (Stata-Corp, TX, USA) was used for statistical analyses. Statistical tests were two-sided, with a significance level set at p < 0.05. Continuous variables were compared using Student’s t-test or the Mann-Whitney U-test after performing the Shapiro–Wilks test. Fisher’s exact test was used to compare discrete variables. Means and standard deviations or medians and interquartile ranges were the main descriptive statistics for continuous variables, while frequencies and percentages were used to report categorical variables. The differences in the values of the variables were compared between the DS and CC groups. Additionally, comparisons were made by dividing all children into the following three age groups: 4−5 years, 6−10 years, and 11−15 years. This age grouping was based on the findings of a previous study on children with DS and CC which showed that younger children’s sleep is developmentally different from teenagers’ sleep [20]. Regarding the assessment of factors for SDB-related signs and symptoms and overnight oximetry-related parameters, we adequately assessed these relationships using regression analysis, and the results were shown as univariate analysis (Model 1) and multivariate analysis (Model 2). Variables with p < 0.10 in the univariate analysis were included in the multivariate analysis. Odds ratios with their
corresponding 95% confidence intervals were reported for the logistic regression analysis, while standardized $\beta$ was reported for the linear regression analysis.

3. Results

3.1. Overall comparisons between children with DS and CC

We evaluated the data from 51 children with DS and 63 CC with acceptable overnight pulse oximetry recordings. Children with DS had a lower body height than that of CC ($p = 0.006$) (Table 1). The body mass index (BMI) was not significantly different between the two groups. Children with DS had more frequent CHD than that of CC ($p < 0.0001$). SDB-related signs and symptoms, such as witnessed midnight arousal, snoring, witnessed apnea, and daytime napping, were more frequently observed in children with DS than in CC ($p = 0.02$, $p = 0.007$, $p < 0.0001$, and $p = 0.003$, respectively). Although the subjective sleeping time did not differ between children with DS and CC, the severity of daytime sleepiness indexed using the ESS was significantly higher in children with DS.

Table 1
Clinical characteristics.

|                      | DS               | CC               | P-value |
|----------------------|------------------|------------------|---------|
| Number               | 51               | 63               |         |
| Age, years           | 8.0 (6.0–12.0)   | 7.0 (5.0–12.0)   | 0.62    |
| Male, N (%)          | 26 (51.0)        | 34 (54.0)        | 0.85    |
| **Physique**         |                  |                  |         |
| Body weight, kg      | 20.0 (16.6–38.0) | 23.6 (18.7–39.0) | 0.07    |
| Body height, cm      | 112.6 (102.0–136.0) | 122.0 (110.0–146.0) | 0.006   |
| BMI, kg/m²           | 16.3 (15.3–19.2) | 16.4 (14.8–18.0) | 0.38    |
| CHD, N (%)           | 35 (68.6)        | 0 (0.0)          | <0.0001 |
| **Questionnaire**    |                  |                  |         |
| Arousal, N (%)       | 29 (56.9)        | 22 (34.9)        | 0.02    |
| Snoring, N (%)       | 29 (58.0)$^a$   | 18 (31.6)$^a$   | 0.007   |
| Apnea, N (%)         | 10 (27.8)$^a$   | 0 (0.0)$^a$      | <0.0001 |
| Napping, N (%)       | 16 (34.0)$^a$   | 6 (9.7)$^a$      | 0.003   |
| ESS, points          | 2.0 (1.0–5.0)    | 1.0 (0.0–2.0)    | 0.0001  |
| Subjective sleeping time, hour | 8.5 (6.9–9.3) | 8.9 (7.7–9.4) | 0.17    |
| **Overnight oximetry** |                  |                  |         |
| Estimated SDB, N (%) | 26 (51.0)        | 9 (14.3)         | <0.0001 |
| 3%ODI, dips/hour     | 5.4 (3.2–7.6)    | 1.6 (0.8–2.6)    | <0.0001 |
| Averaged $\text{SpO}_2$, % | 96.5 ± 0.8       | 97.1 ± 0.9       | 0.004   |
| $\text{SpO}_2<90\%$, % | 5.0 (0.0–10.0)   | 1.0 (0.0–3.0)    | 0.0004  |
| Nadir $\text{SpO}_2$, % | 82.3 (79.2–87.0) | 88.0 (83.0–90.0) | 0.0003  |
| **Sleep postures**   |                  |                  |         |
| Unusual, N (%)       | 27 (52.9)        | 6 (9.5)          | <0.0001 |
| Leaning forward       | 25 (49.0)        | 6 (9.5)          | <0.0001 |
| Sitting               | 9 (19.2)$^a$    | 0 (0.0)$^a$      | <0.0001 |
| Prone, N (%)          | 13 (36.1)$^a$   | 23 (37.7)$^a$    | 0.22    |

DS: Down syndrome, CC: Control children, N: Number, BMI: Body mass index, CHD: Congenital heart diseases, SDB: Sleep-disordered breathing, ESS: Epworth sleepiness scale, ODI: Oxygen desaturation index.

$^a$ Since each answer had missing data (ie, answered as “Unknown”), the denominator of the field differed from the others.

Fig. 1. Unusual sleep postures. (A) Leaning forward with legs back. (B) Leaning forward with legs front. (C) Leaning forward with legs cross. (D) Sitting.
The differences between children with Down syndrome (DS) and control children (CC) in various age groups were examined. Prevalence of estimated sleep-disordered breathing (SDB) in children with DS (p = 0.0001) was higher than in CC. The prevalence of oxygen desaturation index (ODI) was also significantly higher in DS (p = 0.0001). Oxygen saturation (SpO2) parameters measured using pulse oximetry were worse in children with DS (3% ODI, p < 0.0001; average SpO2, p = 0.004; SpO2 <90%, p = 0.0004; nadir SpO2, p = 0.0003). Regarding sleep postures, 52.9% of children with DS had upper airway occlusions (USPs), while only 9.5% of CC had USPs (p < 0.0001). Specifically, the sitting sleep posture was found only in children with DS.

### 3.2. Differences between children with DS and CC in various age groups

Children with DS and CC were stratified into three age groups according to the growing process and different school life systems: 4–5 years, 6–10 years, and 11–15 years. Among these groups, children with DS were divided into 4–5 years (N = 12), 6–10 years (N = 23), and 11–15 years (N = 16), and 63 CC were also divided into 4–5 years (N = 18), 6–10 years (N = 27), and 11–15 years (N = 18) (Table 2) [20]. Body height was significantly lower in children with DS than in CC in all three age groups, and body weight was lower in children with DS than in CC in the age groups 4–5 years and 6–10 years, but the body weights of the children with DS and CC were similar in the age group 11–15 years. Thus, BMI was not significantly different between the children with DS and CC in the age groups 4–5 years and 6–10 years, but the BMI in the children with DS was significantly higher than that in CC in the age group 11–15 years (p = 0.03). Furthermore, a tendency toward obesity was observed after the end of the growth period in body height in children with DS.

Among the SDB-related signs and symptoms, significant differences in witnessed midnight arousal and apnea were not observed between children with DS and CC in the age groups 4–5 years and 6–10 years, but such signs and symptoms were more frequently observed in children with DS than in CC in the age group 11–15 years (73.0% vs. 39.5%, p = 0.045 and 45.5 vs. 0.0%, p = 0.01, respectively). Moreover, overnight pulse oximetry parameters were not significantly different between children with DS and CC in the age group 4–5 years. However, in the age groups 6–10 years and 11–15 years, the ratios of estimated SDB were significantly higher, and other pulse oximetry parameters were significantly worse in children with DS than in CC.

USPs were significantly more frequent in children with DS than in CC in all age groups. USPs were also observed in CC, but their frequency declined along with growth. Children with DS showed no such decline in USPs. Sitting position was observed in 15–25% of children with DS, while none of the CC slept in the sitting position, regardless of age.

Next, we compared differences between pre-pubertal (4–10 years old) and pubertal (11–15 years old) periods in children with DS and CC, separately [Supplementary Table 1]. In the CC, the rate of estimated SDB in pre-pubertal children was significantly higher than that in pubertal children (20.0 vs. 0.0%, p = 0.04). In the children with DS, on the other hand, the significant decreases of SDB-related parameters and USPs noted in CC were not observed, and the reported arousal tended to worsen in the pubertal period. SDB related parameters and USPs were consistently high values in both pre-pubertal and pubertal periods in children with DS.

### 3.3. Factors associated with the presence of SDB

Table 3 shows the factors associated with the SDB-related signs and symptoms, using regression analyses. In the univariate analysis, the presence of DS was significantly associated with witnessed midnight arousal, snoring, daytime napping, and higher ESS values, whereas in the multivariate analysis, the presence of DS was significantly associated with snoring, daytime napping, and higher ESS values (p = 0.007, p = 0.02, and p = 0.001, respectively). Other factors such as male sex, age, BMI, and the presence of USPs were not associated with the SDB-related signs and symptoms in the multivariate analysis.

### Table 2

Differences between children with Down syndrome and typically developing children.

|              | 4–5 years | 6–10 years | 11–15 years |
|--------------|-----------|------------|-------------|
|              | DS        | CC         | P-value     |
| Number       | 12        | 18         |             |
| Age, years   | 4.5 (4.0–5.0) | 5.0 (5.0–5.0) | 0.06        |
| Male, N (%)  | 5 (41.7)  | 8 (44.4)   | 1.00        |
| Physique     |           |            |             |
| Body weight, kg | 14.1 ± 1.9 | 17.7 ± 3.1 | 0.001 |
| Body height, cm | 97.0 ± 7.5 | 107.5 ± 7.7 | 0.001 |
| BMI, kg/m²   | 15.0 ± 1.3 | 15.3 ± 1.4 | 0.05 |
| CHD, N (%)   | 10 (83.3) | 0 (0.0)    | <0.0001 |
| Questionnaire|           |            |             |
| Arousal, N (%) | 6 (50.0) | 7 (38.9) | 0.71 |
| Snoring, N (%) | 6 (50.0) | 6 (33.3) | 0.46 |
| Apnea, N (%)  | 2 (18.2)  | 0 (0.0)    | 0.18 |
| Napping, N (%) | 4 (36.4) | 2 (11.1) | 0.16 |
| ESS, points  | 3.1 (1.0–5.0) | 1.0 (0.0–3.0) | 0.04 |
| Subjective sleeping time, hour | 9.1 (8.5–10.1) | 9.0 (7.1–10.2) | 0.83 |
| Overnight oximetry | | | |
| Estimated SDB, N (%) | 4.3 (33.3) | 6 (33.3) | 1.00 |
| ODI, dips/hour | 4.5 (3.4–8.3) | 2.5 (1.8–5.8) | 0.052 |
| Averaged SpO₂, % | 96.6 ± 0.5 | 97.2 ± 1.0 | 0.12 |
| SpO₂ <90%, % | 6.0 (3.0–10.0) | 3.0 (2.0–16.0) | 0.41 |
| Nadir SpO₂, % | 81.2 (79.0–83.8) | 83.2 (80.5–89.0) | 0.18 |
| Sleep postures | | | |
| Unusual, N (%) | 7 (58.3) | 3 (16.7) | 0.045 |
| Leaning forward | 2 (16.7) | 3 (15.8) | 0.07 |
| Sitting, N (%)  | 2 (16.7)  | 0 (0.0)    | 0.15 |
| Prone, N (%)   | 2 (16.7)  | 5 (27.8)   | 0.67 |

DS: Down syndrome; CC: Control children; N: Number; BMI: Body mass index; CHD: Congenital heart diseases; SDB: Sleep-disordered breathing; ESS: Epworth sleepiness scale; ODI: Oxygen desaturation index.

*Since each answer had missing data (ie, answered as “Unknown”), the denominator of the field differed from the others.*
Regarding the overnight oximetry data, the presence of DS was also significantly associated with a higher prevalence of estimated SDB, higher values of 3% ODI, and lower values of average SpO2 and nadir SpO2, not only in the univariate analysis but also in the multivariate analysis (Model 2: p < 0.0001, p < 0.0001, p = 0.02, and p = 0.003, respectively). However, no significant association was observed between the presence of DS and SpO2 <90% (Table 4). The presence of USPs was significantly associated with a higher value of SpO2 <90%, even after adjusting for potential confounders (p = 0.005).

3.4. SDB-related signs and symptoms and overnight pulse oximetry parameters in children with DS, with or without estimated SDB

The 51 children with DS were further divided into two groups: those with and without estimated SDB (Table 5). Between the two groups, the 3% ODI, average SpO2, SpO2 <90% ratios, and nadir SpO2 were significantly worse in children with DS and estimated SDB (p < 0.0001, p = 0.02, p = 0.0001, and p = 0.009, respectively). However, the presence of USPs was not significantly different between the two groups.

4. Discussion

This case-control study clarified the following: approximately 50% of children with DS had SDB, based on the index of 3% ODI ≥5 dips/h (estimated SDB), while only 14% of CC had SDB; estimated SDB tended to increase in children with DS but decreased in CC along with growth; children with DS had more severe SDB than that of CC, based on the questionnaires and overnight oximetry survey; and children with USPs, which were more frequent in DS, might experience severe hypoxemia caused by SDB.

A previous study using type-1 PSG showed that while 66.4% of children with DS had OSA [21], less than 50% of them who reported sleep problems underwent PSG [22]. Moreover, the former study reported that the prevalence of OSA was 53.8% in children with DS, even in those with a negative history of SDB [21]. These facts imply that many of the children with DS might have missed an appropriate reference timing to improve their sleep quality. The latter study also showed that younger age was associated with more severe SDB, which supported our result that younger age was associated with a higher value of SpO2 <90% (Table 4).

Table 3
Factors for presence of symptoms of sleep-disordered breathing.

Table 4
Factors for presence of estimated sleep-disordered breathing and hypoxicemic status.
SDB in people with DS was associated with reduced cardiac function [9]. To avoid these undesirable effects of SDB on children, early detections of SDB are necessary to ensure better physical and mental development. The American Academy of Pediatrics particularly recommended screening for SDB to manage children with DS [11].

Another study using questionnaires showed that SDB-related signs and symptoms and daytime sleepiness were more frequent in children with DS than in typically developing children [23]. The multivariate analyses in this study also showed that the prevalence of observed snoring and daytime sleeping, including higher ESS values, was higher in children with DS than in CC, only in the age group 11–15 years. The BMI was not significantly different between children with DS and CC in the age groups 4–5 years and 6–10 years but was higher in children with DS than in CC in the age group 11–15 years. Such differences in the BMI between children with DS and CC could lead to a higher rate of observed SDB-related signs and symptoms in children with DS in the age group 11–15 years. Prevention of obesity seems important in DS after the children's heights stop increasing. Previous studies have also shown a close relationship between USPs and SDB-related signs and symptoms, indicating that USPs might alleviate SDB in DS [10,14]. Although it would be possible that USPs alleviate SDB in DS, a significant association was observed only between USPs and accumulated hypoxemia (ie, SpO2 <90%) in the present study, using a multivariate analysis. USPs could have helped avoid airway collapse during sleep [15], but the frequency of USPs was not different between children with DS, with and without estimated SDB (Table 5). The exact reason for these findings were unclear, but it cannot be denied that USPs could provide some protection against SDB (ie, positional therapy) by reducing the severity of SDB in children with DS. Thus, pulse oximetry parameters should be evaluated in terms of sleeping position when the data are recorded. In our study population with DS, the real prevalence of SDB might increase after real-time recordings of both sleeping postures and oximetry parameters.

Our study showed that a high prevalence of estimated SDB, high value of 3% ODI, and low values of average SpO2 and nadir SpO2 were consistently related to the presence of DS after adjusting for several confounding factors. Overnight pulse oximetry is an easy, low-cost, and useful screening tool for SDB in children when PSG is unavailable or difficult to perform owing to intellectual disability [28]. A previous study demonstrated that home pulse oximetry screening could decrease the number of children with DS requiring multichannel sleep studies, and this might substantially reduce the burden on children, families, and health services alike [12].

### 4.1. Limitations

This study had some limitations. First, this was a cross-sectional study that did not allow for the inference of cause and effect. Second, the questionnaire used in this study adopted SDB-related signs and symptoms on the basis of findings from previous studies that have not been standardized or validated for this particular group with DS. Third, we could not perform positional monitoring during pulse oximetry, and thus, we could not assess the direct relationship between USPs and SDB. While the evaluation using PSG would allow us a detailed assessment of SDB, the sleep test using PSG would be difficult in specific types of children, such as young children with severe intellectual disabilities, like those in our study. We consider this a trade-off between a higher quality test in a limited number of patients and a comparably limited quality test in more patients. Taking this point into consideration, we decided to use an oximetry test, which might be advantageous for the young children with severe intellectual disabilities in this study. Since the criteria for evaluating the presence of SDB in children have not yet been established, we used the same criteria as those for adults [4]. This might have resulted in inappropriate diagnoses of SDB in

### Table 5

Differences in Characteristics between DS People with Estimated SDB and Those Without Estimated SDB.

| With SDB | w/o SDB | P-value |
|----------|---------|---------|
| Number   | 26      | 25      | –       |
| Age, years | 8.5 (7.0–12.0) | 7.0 (5.0–10.0) | 0.14 |
| Male, %  | 12 (46.2) | 14 (56.0) | 0.14 |
| Physiology |         |         |         |
| Body weight, kg | 22.0 (17.5–40.0) | 19.0 (15.8–24.0) | 0.09 |
| Body height, cm | 110.0 (100.0–125.5) | 118.5 (108.0–140.0) | 0.056 |
| BMI, kg/m² | 16.4 (15.7–20.4) | 15.7 (15.1–17.8) | 0.22 |
| CHD, N (%)  | 16 (61.5) | 19 (76.0) | 0.27 |
| Questionnaires |         |         |         |
| Arousal, N (%) | 18 (69.2) | 11 (44.0) | 0.07 |
| Snoring, N (%)  | 16 (61.5) | 13 (54.2) | 0.60 |
| Apnea, N (%)  | 7 (43.8) | 3 (15.0) | 0.056 |
| Napping, N (%)  | 6 (24.0) | 10 (45.5) | 0.12 |
| ESS, points  | 2.0 (1.0–4.0) | 2.0 (1.0–5.0) | 0.87 |
| Overnight oximetry |         |         |         |
| Averaged SpO2, % | 96.2 ± 0.9 | 96.8 ± 0.6 | 0.02 |
| SpO2 <90%, % | 17.0 (5.0–26.0) | 3.0 (1.0–4.0) | 0.0001 |
| Prone, N (%)  | 8.06 ± 5.2 | 85.3 ± 4.2 | 0.0009 |
| Sleep postures |         |         |         |
| Unusual, N (%)  | 13 (50.0) | 14 (56.0) | 0.67 |
| Leaning forward | 11 (42.3) | 14 (56.0) | 0.33 |
| Sitting, N (%) | 6 (24.0) | 3 (13.5) | 0.37 |
| Prone, N (%)  | 7 (28.0) | 6 (23.1) | 0.69 |

DS: Down syndrome; SDB: Sleep-disordered breathing; N: Number; BMI: Body mass index; CHD: Congenital heart diseases; ESS: Epworth sleepiness scale; ODI: Oxygen desaturation index.

* Since each answer had missing data (ie, answered as “Unknown”), the denominator of the field differed from the others.
children. The development of specific criteria of SDB for children have not yet been established. To more precisely assess the suitable
cutoff value of pulse oximetry screening when evaluating the
presence of SDB, future studies should investigate the cutoff value,
including its sensitivity and specificity for screening, using over-
night oximetry and monitoring sleeping positions. Since we
recognized that the assessment of SDB using pulse oximetry had
many limitations for the exact diagnoses of SDB, we think that the
future studies based on PSG are mandatory to more precisely assess
SDB and the relationships between USPs and SDB. Additionally, we
obtained SDB-related signs and symptoms from parental replies to
the questionnaires, which inevitably introduces ambiguity,
although this could not be avoided, as it was unlikely for children
with DS to correctly answer the questionnaire by themselves. In
this regard, the use of recently developed screening questionnaires
specifically for SDB in children with DS would have been valuable
[29]. We could not obtain data regarding the levels of intellectual
disability in conjunction with the International Classification of Diseases 10th Editions Clinical Modification (ICD-10) in the
children with DS participating our study since the questionnaires were
completed by their caregivers, who were non-medical personnel.
We think that it would be difficult for parents to judge objective
intellectual disability levels, classified by the ICD-10 code, for their
children with DS. Despite these limitations, the population-based
sampling frame improved the external validity of the study
findings when compared with those of studies conducted only among
patients with DS. The use of the Epworth Sleepiness Scale for
Children and Adolescents (ESS-CHAD) might overcome this problem
and be more useful for assessing excessive daytime sleepiness
in this particular population [30]. However, we could not use ESS-
CHAD in this study since the study began in 2015 when the Japa-
nese version of ESS-CHAD had not yet been developed. In the
parental reports of signs of daytime sleepiness, a higher rate of
daytime napping (28–40%) than that of the self-reports of ESS in
children with DS was observed. We believed that parental reports
would be reliable compared with the results of ESS in those chil-
dren since we did not use ESS-CHAD. The parental reports indicated
that children with DS might frequently have sleep-related prob-
lems, such as SDB, and the problems might worsen their daytime activations. We recognized this as a limitation of the study, but
parental recognition of the high rates of daytime napping in chil-
dren with DS might be important to manage the children. It is well
known that the presence of SDB is associated with the presence of
snoring or apnea. We excluded this variable from Model 2 because of
multicollinearity. Lastly, we could not confirm the reliability of
overnight pulse oximetry examinations using PSG. While the
evaluation using PSG enabled us to assess SDB-related data in
detail, the sleep test using PSG would be difficult in some children,
such as young children with severe intellectual disabilities who
might be present in the group of children with DS. The difficulty of
PSG would lead to a significant selection bias in this study. Thus, we
used an oximetry test, which might be advantageous for young
children with severe intellectual disabilities.

5. Conclusions

Our study showed that SDB was more prevalent and severe in
children with DS than in CC, and the difference in prevalence
came more obvious with age. The children with USPs, who were
more frequent in cases of DS, might suffer from more severe hyp-
oxemia due to SDB than those without USPs. More attention should
also be paid to children with DS, especially those with USPs, for the
early detection and treatment of SDB. This study indicated the high
prevalence of SDB in children with DS compared with CC and aimed to
detect SDB with the combination of overnight pulse oximetry
examination and parental reports of SDB-related signs, including
the USPs. This assessment might be useful for early detection of
SDB, especially in children with intellectual disabilities who might
not be able to participate in repetitive or formal sleep tests.

Authorship statement

H.S., A.R., M.N., S.A., and A.C. were contributed to "Study Design". H.S., A.R., N.M., K.F., and N.H. were contributed to "Data Collection". H.S. and A.R. were contributed to "Analyzing data/Writing the pa-
per". All authors were contributed to "Interpretation of data/ Revising the manuscript critically for important intellectual content".

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Conflict of interest

None declared.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the
following link: https://doi.org/10.1016/j.sleepx.2022.100045.

Appendix A Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleepx.2022.100045.

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