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Research Article

Retrospective analysis of sleep-disordered breathing in pediatric neuromuscular disease

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ABSTRACT

Objective: Sleep-disordered breathing (SDB) is a prevalent concern in individuals with neuromuscular diseases (NMD), significantly impacting respiratory function and sleep quality. This study aimed to retrospectively evaluate the demographic, clinical, and baseline polysomnographic data of children with NMD to investigate the guiding effect of the Pediatric Sleep Questionnaire (PSQ) and the modified Epworth Sleepiness Scale (ESS-CHAD) in detecting SDB.

Method: A retrospective analysis was conducted on children aged 2-18 years with NMD who underwent polysomnography (PSG) between January 2012 and January 2024. The study assessed various clinical parameters, including age, gender, BMI, underlying disease, PSG results, the PSQ and ESS-CHAD scores, and treatment methods. Statistical analyses were conducted to compare those with and without obstructive sleep apnea syndrome (OSAS).

Results: Of the 174 patients included in the study, 90 patients (51.7%) had normal PSG, 56 patients (32.2%) had mild (OSAS), 12 patients (6.9%) had moderate OSAS, and 16 patients (9.2%) had severe OSAS. PSQ and ESS-CHAD were not significantly different between patients with and without OSAS ($p>0.05$). The most common treatment initiated was noninvasive ventilation (NIV), recommended for 23% of patients.

Conclusion: PSG is the gold standard for diagnosing SDB in children with NMD. While PSQ and ESS-CHAD may be useful for screening in the general pediatric population, they are inadequate in identifying OSAS in children with NMD. Early diagnosis and treatment of SDB are crucial for improving outcomes in this patient group.

Keywords: sleep-disordered breathing, neuromuscular diseases, polysomnography, pediatric sleep questionnaire

INTRODUCTION

Sleep-disordered breathing (SDB) is a group of conditions characterized by abnormal breathing patterns during sleep, affecting both adults and children.[1] SDB represents a significant concern in individuals with neuromuscular diseases (NMD), impacting both respiratory function and sleep quality. Individuals with NMD often face respiratory complications due to weakness of respiratory muscles, leading to an increased risk of SDB.[1]

Untreated SDB can result in cardiovascular side effects, metabolic disorders, and neurocognitive issues, all of which can be exacerbated by innate NMD symptoms.[2] Cognitive impairments, attention deficit/hyperactivity disorders, and social disabilities that may be difficult to cope with have

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been reported in SDB that are not detected early and treated.[3] Therefore, SDB should be screened and treated early in children with NMD.

Polysomnography (PSG), the gold standard for assessing SDB, offers valuable insights into respiratory and sleep parameters.[1] However, PSG is time-consuming, technician-dependent, and not widely accessible.[4] Consequently, pediatric prediction tools for SDB aim to detect obstructive sleep apnea syndrome (OSAS) and identify children needing further evaluation.[4] The Pediatric Sleep Questionnaire (PSQ) and the modified Epworth Sleepiness Scale (ESS-CHAD) serve as reliable SDB screening tools.[5] The PSQ demonstrates 85% sensitivity and 87% specificity for detecting PSG-confirmed SDB in healthy children aged 2-18 years.[5] The ESS-CHAD, a self-report questionnaire, assesses daytime drowsiness in eight daily scenarios.[6] Initially validated for OSAS patients, it is now widely used to identify various conditions causing excessive sleepiness in the general population.[7]

This study aimed to retrospectively evaluate the demographic, clinical, and baseline polysomnographic data of children with NMD to investigate the guiding effect of PSQ and ESS-CHAD in detecting SDB.

METHODS

We analyzed children aged 2-18 years with NMD who underwent PSG in our pediatric sleep laboratory between January 2012 and January 2024. Clinical data, including age, gender, BMI, underlying disease, PSG indications, the result of carbon dioxide in venous blood gas, and treatment methods were collected. Ethics committee approval was obtained from the ethics of Marmara University (Protocol no:28.06.2024.757). Parental informed consent was obtained for the patients.

Polysomnography

Polysomnography (Alice 5, Respironics, Murrysville, PA) was performed to assess respiratory parameters, sleep architecture, and treatment modalities. The following instruments were employed: electroencephalogram (EEG), electrooculography (EOG), chin and diaphragm electromyograph (EMG), thoracic and abdominal effort respiratory inductance plethysmography (RIP) bands, nasal airflow, thermistor, body position, electrocardiogram (ECG), SpO2, and a complete audio and video recording. The PSGs were manually scored by a qualified pediatric sleep physician using the American Academy of Sleep Medicine (AASM) 2012 pediatric criteria.[1,8] The apnea-hypopnea index (AHI) was calculated by dividing the total number of obstructive, central, and mixed apneas and hypopneas by the number of hours of uninterrupted sleep.[8] Obstructive AHI (oAHI) was determined by measuring the total number of obstructive apnea and hypopnea events per hour of sleep, and the oxygen desaturation index (ODI) was measured by the number of oxygen desaturations of P3% per hour of sleep.[8] Based on the patients' oAHI, the severity of OSAS was assessed.[8,9] When the oAHI is ≤ 5 events per hour but >1 event per hour, it is considered mild; when it is ≥5 events per hour but ≤ 10 events per hour, it is considered moderate; and if it is >10 events per hour, it is considered severe.[8,9] When the central apnea index (CAI) is >5 events per hour, central apnea is diagnosed.[8,9] The normal value of carbon dioxide in venous blood gas in children is usually between 35 and 45 mmHg, and above 45 mmHg was considered carbon dioxide retention.[10]

Pediatric sleep questionnaire

The Pediatric Sleep Questionnaire (PSQ) is designed to assess breathing disorders related to sleep-related symptoms.[5] This parent-reported survey includes 22 questions about snoring, observed apneas, difficulty breathing while sleeping, and other characteristics of OSAS. For pediatric SDB, a threshold of 0.33 is used to determine elevated risk.[5]

The modified epworth sleepiness scale

The Modified Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD) is a validated, simple scale including eight questions with four-point Likert scale answers and aims to assess excessive daytime sleepiness (EDS) for children> 12 years old.[6,11] The ESS-CHAD score, which ranges from 0 to 24, reflects the degree of sleepiness, with higher scores indicating greater sleepiness. Scores exceeding 10 suggest excessive daytime sleepiness and potential underlying sleep disorders.[6]

Statistical analysis

Analyses were performed using Statistical Package for the Social Sciences (version 16.0; SPSS Inc.; Chicago, IL, USA). Demographic and clinical information for all patients were reported using mean and standard deviation for continuous variables and median with interquartile range. For categorical variables, frequencies and percentages were used. The Mann–Whitney U and Kruskal–Wallis tests were used to compare the study groups for data that did

not follow a normal distribution. Additionally, a chi-square test was used to compare the differences in proportions between the two independent groups. Statistical significance was set at $P < 0.05$.

RESULTS

Baseline PSG was performed in 174 patients during the study period. The median age was 10 years (25-75p, 5.1-13.5), and 124 patients (71.3%) were male. Fifty-four (31%) patients had Duchenne muscular dystrophy (DMD), 23 (13.2%) had spinal muscular atrophy (SMA), and 64 (36.8) had other myopathies. The most common indication for PSG was pCO2 retention in venous blood gas analysis, and 49 (28.2%) patients underwent PSG to assess OSAS symptoms, including snoring and open mouth breathing. Table 1 shows the clinical and demographic characteristics of all patients as well as groups according to the presence of OSAS.

According to the oAHI, 90 patients (51.7%) had normal PSG, 56 patients (32.2%) had mild OSAS, 12 patients (6.9%) had moderate OSAS, and 16 patients (9.2%) had severe OSAS. Eight patients also had central apnea, seven of whom had mixed apnea.

No statistically significant differences were observed in PSQ scores between individuals with and without OSAS. Similarly, for patients aged ≥ 12 years, ESS-CHAD scores demonstrated no significant variation between those diagnosed with OSAS and those without the condition. There was no significant difference between those with and without OSAS in terms of age, sex, BMI, and blood venous gas PCO2 results. The median AHI, OAHI, and ODI were significantly higher in the subjects with OSAS than those without OSAS ($p<0.005$). In both groups, with and without OSAS, REM stage AHI, OAHI, and ODI were higher compared to the non-REM stage. However, the differences were not statistically significant in either group ($p>0.005$).

Table 2 lists the respiratory and sleep parameters of all patients. The median OAHI was found to be 0.85 (25-75p, 0-3.1). The median OAHI was significantly higher (1.7, 0.1-3.7) in patients with OSAS symptoms compared with those

Table 1. Demographic and clinical features of the patients (n: 174)	
Age (years), median (25-75p)	10 (5.1-13.5)
Male, n (%)	124 (71.3)
Body Mass Index, median (25-75p)	17.9 (13.9-20.8)
Blood venous gas PCO_2 (mm-Hg), mean±SD	45.7±9.1
PSQ, median (25-75p)	0.28 (0.13-0.45)
ESS-CHAD, median (25-75p)	3 (1-6)
The underlying disease of the patients	
* Duchenne muscular dystrophy, n (%)	54 (31)
* Myasthenia gravis, n (%)	26 (14.9)
* Spinal muscular atrophy, n (%)	23 (13.2)
- Spinal muscular atrophy Type 2, n (%)	14 (8)
- Spinal muscular atrophy Type 1, n (%)	8 (4.6)
- Spinal muscular atrophy Type 3, n (%)	1 (0.6)
* Peripheral neuropathies, n (%)	7 (4)
* Other myopathies n (%) (congenital, metabolic, and other dystrophies, etc.)	64 (36.8)
PSG indications	
*pCO_2 retention in venous blood gas analysis, n (%)	52 (29.9)
*Snoring and open mouth breathing, n (%)	49 (28.2)
*Evaluation of respiratory muscle involvement due to neuromuscular disease without any complaint n (%)	43 (24.7)
*Witnessed apnea, n (%)	20 (11.5)
*Pre-decannulation evaluation, n (%)	6 (3.4)
*Evaluation for desaturation, n (%)	4 (2.3)

PSQ, pediatric sleep questionnaire; ESS-CHAD, modified epworth sleepiness scale; PSG, polysomnography

Table 2. Respiratory and sleep parameters from PSG (n: 174)	
AHI, median (25-75p)	1.65 (0.6-3.7)
CAI, median (25-75p)	0.3 (0-0.9)
OAHI, median (25-75p)	0.85 (0-3.1)
ODI, median (25-75p)	1.9 (0.6-5.8)
The lowest O2 saturation, median (25-75p)	92 (88.5-94)
N1 Ratio, median (25-75p)	3.7 (1.7-8.2)
N2 Ratio, median (25-75p)	53.5 (44.9-59.1)
N3 Ratio, median (25-75p)	33.5 (25-41.5)
REM Ratio, median (25-75p)	5.2 (0.2-12.7)
TST, median (25-75p)	354.1 (213-414)
WASO, median (25-75p)	30 (8.8-60)
SL, median (25-75p)	19.1 (9.4-37.9)
SE, median (25-75p)	83.7 (71.5-92)
REM Latency, median (25-75p)	129.5 (81.7-216.7)

PSG, polysomnography; AHI, apnea-hypopnea index; CAI, central apnea index; OAHI, obstructive apnea-hypopnea index; ODI, oxygen desaturation index; REM, rapid eye movement sleep; TST, total sleep time; WASO, waking up after sleep onset; SL, sleep latency; SE, sleep efficiency

with no OSAS symptoms (0.6, 0-2.4) (p=0.044). Among the patients who underwent PSG because of pCO2 retention in venous blood gas analysis (n:37), mild OSAS was found in 11 patients and severe OSAS was found in two patients. However, PSG results of 24 patients were normal.

The study's primary patient groups were DMD, SMA type 2, and myasthenia gravis (MG). The MG group had younger patients and higher BMI, but the difference was insignificant (p>0.05). OSAS was found in 59.2% of DMD patients, 55.5% of SMA type 2 patients, and 46.1% of MG patients, with no significant difference between groups (p>0.05). Age, PSQ and ESS-CHAD scores, BMI, and blood venous gas pCO2 results showed no significant differences across the groups (p>0.05), except for gender (p=0.007). Additionally, no significant differences were noted in other PSG parameters (p>0.05).

PSQ and ESS-CHAD scores did not exhibit statistically significant differences between DMD and MG patients with and without OSAS (p>0.05) (Table 3). In patients with DMD who were diagnosed with OSAS, age was significantly higher, and the venous blood gas pCO2 value was significantly elevated and exceeded 45mmHg (p<0.05) (Table 3).

After the study, treatment was initiated in 25.3% of patients (n=44). The most recommended treatment method was noninvasive ventilation (NIV) (n=37, 21.3 %). One of the six patients with a decannulation plan was decannulated, and the remaining five patients continued invasive ventilation (Table 4).

DISCUSSION

Our investigation revealed that SDB is common in patients with NMD. The PSQ and ESS-CHAD provided inadequate for diagnosing OSAS in NMD patients. PSG remains the most reliable diagnostic tool for SDB. Despite PSG being the gold standard, there is ongoing exploration of alternative diagnostic methods due to the limited availability of PSG-equipped sleep centers and the need for specialized expertise. As a result, symptom scores and questionnaires have often been used but are insufficient for detecting SDB.

Children with NMD frequently have a higher incidence of SDB compared to the general population, with estimates ranging from 27% to 62%.[12,13] Labanowski et al. reported a 42% prevalence of SDB in their study of children and adults with NMD.[14] Oros et al. found an 80.5% rate of OSAS, attributing the higher rate to PSGs conducted during the second decade of life and respiratory failure from scoliosis.[3] Our study identified OSAS in 48.3% of patients, consistent with previous findings.[13,14]

Table 3. The characteristics of DMD and MG patients with and without OSAS (n: 80)						
	Duchenne muscular dystrophy (n:54)			**Myasthenia gravis (n:26)**		
	OSAS + (n: 32)	**No OSAS (n: 22)**	**P value**	**OSAS + (n: 12)**	**No OSAS (n: 14)**	**P value**
Age (years), median (25-75p)	12.7 (10.1-14.5)	8 (7.2-11.1)	0.000*	5.5 (3.5-12.7)	7.9 (3.9-14.9)	0.410
Male/female	31/1	18/4	0.063	9/3	7/7	0.200
BMI, median (25-75p)	17.9 (14.8-22.3)	17.9 (14.9-22.7)	0.740	20.3 (17-22.7)	23 (18.7-24.5)	0.272
Blood venous gas PCO_2 (mm-Hg), mean±SD	47.8±6.4	41.8±8	0.046*	46.4±6.6	46.9±4.9	0.863
PSQ, median (25-75p)	0.2 (0.1-0.4)	0.2 (0-0.4)	0.965	0.1 (0-0.3)	0.2 (0.1-0.5)	0.347
ESS-CHAD[a], median (25-75p)	2.5 (0-6)	2 (0-6)	0.817	1 (0-4)	6 (1-9)	0.092

Duchenne muscular dystrophy, DMD; Myasthenia gravis, MG; BMI, Boddy Mass Index; PSQ, pediatric sleep questionnaire; ESS-CHAD, modified Epworth Sleepiness Scale; OSAS, obstructive sleep apnea; * Mann-Whitney U test, [a]: for aged ≥ 12 years (n: 29)

Table 4. Treatment modalities of the patients (n: 44)	
	n (%)
Noninvasive ventilation (NIV)	37 (21.3)
* Duchenne muscular dystrophy, n (%)	12 (32.4)
* Spinal muscular atrophy type 2, n (%)	3 (8.2)
* Myastenia gravis, n (%)	4 (10.8)
* Other myopathies n (%) (congenital, metabolic, and other dystrophies etc.)	12 (32.4)
* Others, n (%)	6 (16.2)
Continuation of Invasive Ventilation, n (%)	5 (2.9)
Decannulation, n (%)	1 (0.6)
Supplemental Oxygen, n (%)	1 (0.6)

The PSQ has shown differing efficacies in detecting OSAS across various patient groups. In healthy children, it demonstrated high sensitivity for moderate OSAS.[15] Bamaga et al. found that the PSQ detected OSAS in 36.7% of children with DMD.[16] In our center's comorbid patients, the PSQ's sensitivity and specificity were 71.8% and 40.4%, respectively.[17] EDS is a key OSAS symptom in adults, and the ESS is a validated screening tool for this condition.[18] However, EDS is not common in children, and ESS-CHAD does not correlate with pediatric OSAS.[19] Our study found that PSQ and ESS-CHAD were inadequate for predicting OSAS in children. While the PSQ is effective for screening healthy children, it was less successful in identifying those with underlying diseases.[20] Solis et al.'s findings in syndromic patients also support our results.[21]

DMD and SMA patients exhibited a higher incidence of pediatric OSAS compared to healthy controls.[22,23] Chacko et al. noted that SMA types 1 and 2 are more prone to SDB, while type 3 is less affected.[24] Our patient group, primarily with SMA type 2, similarly showed a higher occurrence of OSAS (55.5%). Suresh et al. found OSAS in 31% of DMD patients, whereas our study detected it in 59.2% of DMD patients.[25] Our study detected OSAS in 59.2 % of DMD patients. The higher OSAS rate in our study may be due to the use of PSG in younger patients (first decade), which increases detection rates. Conversely, Suresh's study mainly performed PSG in patients in their second decade of life, noting a higher frequency of nocturnal hypoventilation.

Respiratory muscle involvement in DMD worsens with age. Our study found that DMD patients with OSAS were older than those without OSAS. M. Romei et al. also noted age-related increases in respiratory muscle involvement.[26] Additionally, pCO2 retention in venous blood gas may indicate respiratory muscle involvement in NMD. In our study, DMD patients with OSAS had venous blood gas pCO2 values exceeding 45 mmHg. Hukins et al. identified a venous blood gas pCO2 value ≥45 mmHg in DMD patients as a sensitive and specific indicator of SDB.[27] These findings suggest that respiratory muscle involvement may begin around age 10 years, coinciding with the expected loss of ambulation, indicating the need for PSG at this age.[28]

In patients with NMD, SDB may develop prior to the onset of respiratory failure symptoms and present as daytime hypercapnia.[29] In our study, the most common indication for PSG was pCO2 retention in the venous blood gas analysis, and this indication was most common in the SMA group. Labanowski et al. reported that nocturnal hypoventilation and daytime hypercapnic respiratory failure are frequently observed in patients with NMD, particularly in SMA type 2 patients.[14] Although the most common indication was pCO2 retention in our patients, PSG findings were normal in 26 patients. This may be because capnography cannot be performed simultaneously with PSG, and nocturnal hypoventilation cannot be evaluated.

Noninvasive ventilation (NIV) is crucial for managing respiratory involvement in NMD.[30] In our study, 25.2% of patients received treatment, with NIV being the most common method. Oros et al.'s study on 108 NMD patients showed a higher NIV rate of 36.8%.[3] The lower treatment rate compared to the OSAS rate is due to the mild OSAS patient group being ambulatory, young, and under close monitoring. There are no established clinical criteria for initiating NIV support for NMD. Thus, close monitoring and NIV initiation based on clinical suspicion are planned for these patients.[12]

Our retrospective study may have limitations, such as incomplete patient data and a small number of individuals with specific conditions like myopathies. Nonetheless, the

findings could guide the design of future, more refined research.

CONCLUSION

Our single-center study indicates that the PSQ and ESS-CHAD are ineffective for identifying SDB in children with NMD, with PSG remaining the gold standard for diagnosis. OSAS is a significant and common condition in pediatric NMD patients, exacerbating symptoms and diminishing quality of life. Early diagnosis and treatment of OSAS are crucial, necessitating a comprehensive understanding of its diagnosis, technology, prognosis, and long-term care.

Ethical approval

This study has been approved by the Marmara University Ethics Committee (approval date 28.06.2024, number 2024.757). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: MYK, APE, EEE; data collection: EEB, FÖ, MAY, CAY, NMÇ, MS, ŞK; analysis and interpretation of results: MYK, EEE, YG, BK; draft manuscript preparation: MYK. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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