Demographics and Disease Characteristics Among Pediatric Patients With Narcolepsy

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INTRODUCTION

- Narcolepsy is a rare, chronic sleep disorder with symptom onset typically occurring between the ages of 10 and 25 years[1,2]
- While symptom onset most commonly occurs in adolescence or young adulthood, diagnosis of narcolepsy may be delayed 10 years or more[3-7]
- Narcolepsy type 1 (NT1) and type 2 (NT2) are differentiated by the presence of cataplexy in NT1[2]
  - Among adults, recent claims database analyses estimate about 2/3 of narcolepsy diagnoses are NT2[8]
  - In pediatric patients, sleep clinicians generally estimate a greater proportion of NT1
- The most recent 2021 American Academy of Sleep Medicine (AASM) clinical practice guidelines have no strong recommendations for the treatment of narcolepsy in pediatric patients and conditional recommendations for only sodium oxybate (SXB) and modafinil[9]
  - In the prior 2007 AASM Practice Parameters, methylphenidate and modafinil were recommended as options for children with narcolepsy[10]
- In recent years, several medications have been approved for the treatment of narcolepsy in pediatric patients (ie, SXB [2018]; mixed-salt oxybates [2021]; pitolisant [2024]; extended-release, once-nightly SXB [2024])[11-14]
- Given the lack of available data, clinical and demographic information of pediatric patients with narcolepsy is needed to better understand this population, including the prevalence of narcolepsy subtypes, time to diagnosis, comorbidities, and treatment patterns

OBJECTIVE

- To understand the characteristics of pediatric narcolepsy including demographics, comorbidities, time to diagnosis, and treatment use

METHODS

DATA SOURCE AND PATIENTS

- A retrospective review of registry data from patients at 22 US hospitals between 2009 and 2017 was conducted
  - Data collected included: demographic information, medical history (eg, age of onset of each symptom, existence of streptococcus and other infections, injuries, other associated disorders), results of laboratory and other diagnostic tests (eg, genetic marker for narcolepsy), polysomnography (PSG) and multiple sleep latency test (MSLT) findings, and therapies (pharmacologic and non-pharmacologic)
- Data were included from patients who:
  - Were aged ≤18 years
  - Were diagnosed with NT1 or NT2
  - Underwent a clinical evaluation and overnight PSG study with an MSLT

DATA ANALYSIS

- Given that the study was designed for hypothesis generation and not statistically powered for comparisons between groups, all data were analyzed descriptively

RESULTS

PATIENT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

- A total of 471 patients were identified from the Pulse Infoframe registry of 950 patients (**Table 1**)
  - Patient sex was evenly distributed
  - Most patients were non-Hispanic and had a diagnosis of NT1
- Among patients with a known Tanner stage score at the time of diagnosis, the most common classifications were stage 1, followed by stage 5 (**Table 2**)

TABLE 1: Patient Demographics and Clinical Characteristics

Characteristic, n (%)	Overall (N=471)
Sex	
Female	224 (48)
Male	247 (52)
Race	
American Indian or Alaska Native	1 (<1)
Asian	9 (2)
Black or African American	194 (41)
Caucasian or white	227 (48)
Mixed or >1 race	12 (3)
Pacific Islander	2 (<1)
Other	18 (4)
Unknown	8 (2)
Ethnicity	
Hispanic	24 (5)
Not Hispanic	421 (89)
Unknown	26 (6)
Narcolepsy subtype[a]	
NT1	331 (70)
NT2	139 (30)
Unknown	1 (<1)

[a]Narcolepsy subtypes were defined as follows: NT1, patient has cataplexy; NT2, patient does not have cataplexy; unknown, it is unknown whether the patient has cataplexy. NT1, narcolepsy type 1; NT2, narcolepsy type 2.

TABLE 2: Tanner Stage Score at Time of Diagnosis

Tanner score, n (%)	Overall (N=471)
Stage 1	79 (17)
Stage 2	31 (7)
Stage 3	32 (7)
Stage 4	39 (8)
Stage 5	55 (12)
Not done[a]	187 (40)
Missing or unknown[a]	48 (10)

[a]Tanner stage score was not reported for approximately half of patients.

TIME TO DIAGNOSIS

- The median (IQR) age of excessive daytime sleepiness (EDS) symptom onset was 9.0 (6.9, 12.5) years (**Figure 1**)
- The median time from EDS onset to narcolepsy diagnosis was 3.0 years

FIGURE 1: Age at EDS Onset and Narcolepsy Diagnosis

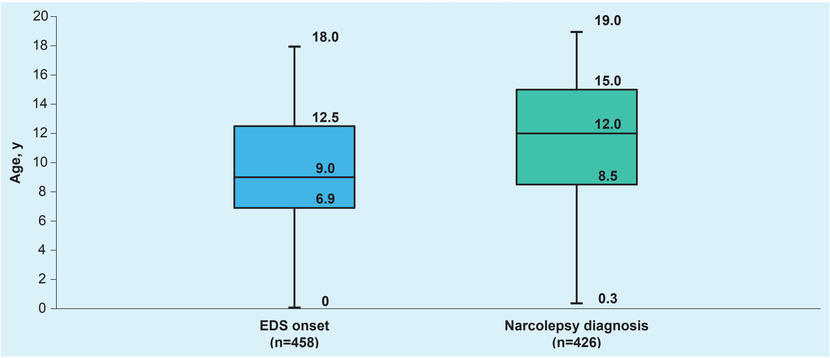


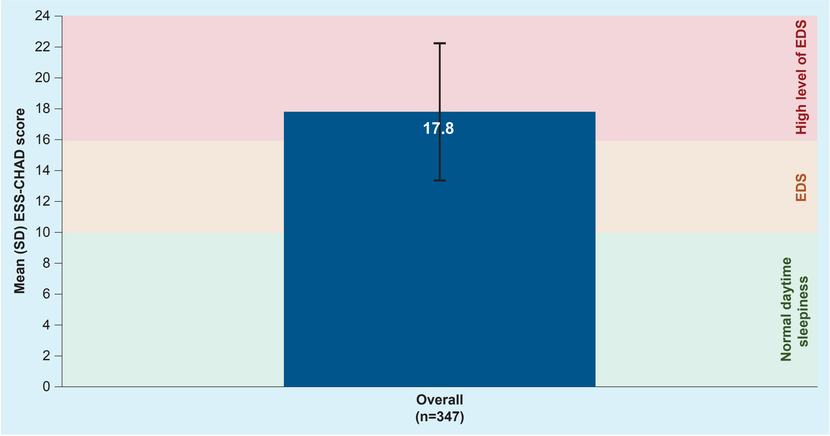
Figure displays median, IQR, and range.
EDS, excessive daytime sleepiness; IQR, interquartile range.

DISEASE CHARACTERISTICS

Severity of EDS

- The Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD),[15] an 8-item scale used to evaluate EDS, is similar to the adult ESS[16] but with minor adaptations to assess how likely a child or an adolescent is to doze off or fall asleep while:
  - Sitting and reading
  - Sitting and watching TV
  - In a classroom at school during the morning
  - As a passenger in a car for about 30 minutes without a break
  - Lying down to rest in the afternoon
  - Sitting and talking to someone
  - Sitting by themselves at lunch
  - As a passenger in a car while stopped for a few minutes in traffic
- Before receiving any treatment, mean (SD) ESS-CHAD score was 17.8 (4.5), indicating a high level of EDS (**Figure 2**)

FIGURE 2: ESS-CHAD Scores Before Treatment[a]



ESS-CHAD scores of 0 to ≤10, >10 to <16, and ≥16 to 24 indicate normal daytime sleepiness, EDS, and a high level of EDS, respectively.[16]
EDS, excessive daytime sleepiness; ESS-CHAD, Epworth Sleepiness Scale for Children and Adolescents.
[a]Three ESS-CHAD scores were excluded owing to not being within the allowed set of values (23.5, 26.0, 30.0).

Sleep-Related Symptoms

- In addition to cataplexy, >50% of pediatric patients were described as restless sleepers and experienced sleep maintenance problems, sleep talking, and snoring (**Table 3**)

TABLE 3: Sleep-Related Symptoms[a]

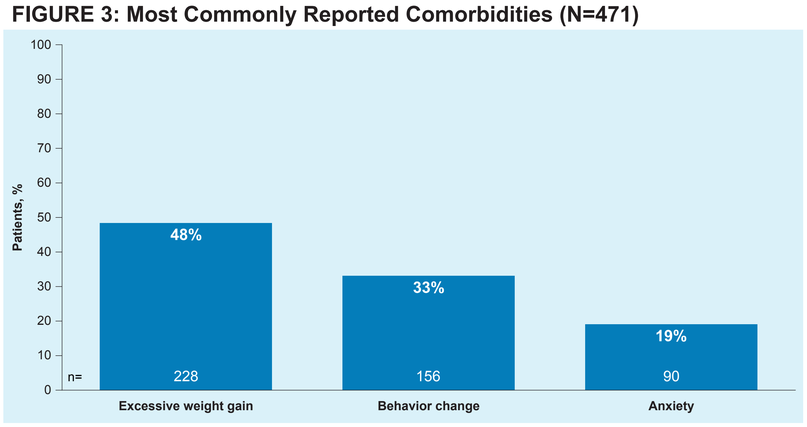
Symptom, n (%)	Overall (N=471)
Cataplexy	331 (70)
Restless sleep/restless sleeper	295 (63)
Sleep maintenance problems	275 (58)
Sleep talking	270 (57)
Snoring	256 (54)
Leg jerking/leg kicking/jerking	228 (48)
Hypnagogic hallucination(s)	220 (47)
Nightmares	172 (37)
Restless leg disorder/periodic limb movement disorder	171 (36)
Sleep paralysis	160 (34)
Sleep onset problem	86 (18)
Sleepwalking	80 (17)
Snorting/gasping	73 (15)
Teeth grinding	71 (15)
Pauses	71 (15)
Night terrors	70 (15)
Bedwetting	53 (11)

[a]Sleep-related symptoms were assessed at the time of diagnosis for all listed symptoms except for cataplexy (assessed either before or after diagnosis) and hypnagogic hallucination(s) and sleep paralysis (assessed at the time of questionnaire completion).

Comorbidities

- The top 3 most commonly reported comorbidities among pediatric patients with narcolepsy were excessive weight gain, behavior change, and anxiety (**Figure 3**)

FIGURE 3: Most Commonly Reported Comorbidities (N=471)



Treatments

- More than half of patients had ever previously tried a stimulant (88%), a wake-promoting agent (69%), or an antidepressant (51%) at some point in the past (**Figure 4**)
- Approximately 1 in 3 patients (31%) had ever tried SXB

FIGURE 4: Prior Treatments (N=471)

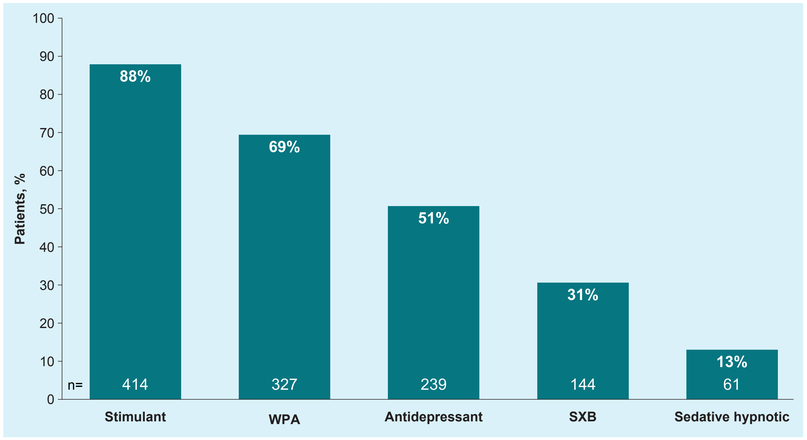


Figure includes treatments that had ever been previously tried.
SXB, sodium oxybate; WPA, wake-promoting agent.

STUDY LIMITATIONS

- The registry data from 2017 do not reflect current treatment practices
- The frequency of missing data reduces the representativeness of the sample and the ability to draw conclusions

CONCLUSIONS

- NT1 was a more prevalent diagnosis than NT2 in this cohort of pediatric patients who underwent overnight PSG with an MSLT
- There was a wide range in age of patients at diagnosis and no observed relationship with Tanner stage score
- The reasons for the shorter diagnostic delay in pediatric patients (3 years) than that reported in adults (10 years) require further investigation
  - Comorbidities, such as excessive weight gain and behavior changes, were common and may contribute to this diagnostic delay
- Since the time of this analysis, approval of SXB and new formulations of SXB provide clinicians with broader options to treat patients

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DISCLOSURES

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JO has served as a consultant to AGB Pharma (Sweden) and on an Independent Safety Monitoring Board for Idorsia Pharmaceuticals.

LEO has served on advisory boards for Avadel Pharmaceuticals, Harmony Biosciences, and Jazz Pharmaceuticals.

GF and **NS** have no competing interests to disclose.

JH and **FHG-S** are employees of Pulse Infoframe.

JG was an employee of Avadel Pharmaceuticals and is a consultant to Alkermes, Inc.

BA is an employee of Alkermes, Inc.