Narcolepsy is primarily a sleep disorder and one of the most important causes of excessive daytime sleepiness in children. Diagnosis is often delayed by up to 12 years, as its signs and symptoms are often confused with other conditions and because of the absence of easily measurable biomarkers. Two types of narcolepsy exist, narcolepsy with cataplexy or type 1 (NT1), and narcolepsy without cataplexy or type 2 (NT2). Cataplexy is characterized by one or more sudden short-term (≤2 minutes) attacks of muscle tone (often due to an emotional trigger), yet it is rarely observed in children. Few studies to date have compared pediatric patients with NT1 and NT2, including demographic characteristics and treatment patterns.

OBJECTIVES

• Compare demographic and clinical characteristics of pediatric patients prior to diagnosis with NT1 and NT2.
• Compare narcolepsy recommended treatment rates within 1 year post-diagnosis among patients diagnosed with NT1 and NT2.

METHODS

Study Design: Prospecively recruited age-matched cohort study

Data Source:
• TriNetX EMR Research Data Network
• A federated EMR network of 26 academic medical centers, physician specialties, and specialty hospitals across the U.S. treating a total of 3.4 million patients

Patient Selection:
• Patients aged ≤17
• Diagnosis of NT1 (ICD-10: G41.41, G41.42) and no evidence of NT2 (G41.49, G41.492) or NT2 alone on ≥2 visits at least 1 month to 1 year apart

Baseline Characteristics:
• Demographics – age, sex, race
• Symptoms using ECD-CM codes
• Sleep study use 1 year before diagnosis (index) – CPT4 codes

Outcomes:
• Recommended prescription drug use 1 year post diagnosis

Statistical Analysis:
• Test and chi-square tests as appropriate for baseline characteristics
• Odds ratios (OR) and 95% CI for post-index prescription drug use
• All analyses conducted using the TriNetX Analytics Platform

RESULTS

Patient Demographics:
• Pediatric study cohorts consisted of 115 NT1 and 299 NT2 patients (Table 1).
• The racial distributions of the NT1 and NT2 cohorts differed significantly:
  – The proportion of white patients in the NT1 cohort being more than 2x that of black patients (56% vs 25%)
  – Similar proportions of NT2 patients being black (42.5%) or white (42.1%)
• NT2 patients were diagnosed at an older age than NT1 patients 11.3 ± 3.5 vs 10.1 ± 4.4 years, P<0.001

Pre-Narcopal Symptom and Associated Diagnoses:
• While not significantly different, pre-index symptoms of narcolepsy – snoring (R06.83: 21.4% vs 17.7%), malaise and fatigues (R33: 13.4% vs 10.4%), behavioral and emotional disorders (F90: F90: 12.4% vs 8.7%), and asthma (J45: 13.7% vs 8.7%) were greater in NT2 compared to NT1.
• Lack of expected physiologic development (R26: 4.3% vs 8.7%) was about half the prevalence in NT2 compared to NT1, but did not reach statistical significance, P=0.094.
• The prevalence of oppositional defiant disorder was significantly lower for NT2 compared to NT1 (3.3% vs 8.7%; P=0.023).
• For NT2 compared to NT1 patients, there were no differences in the periodic breathing (R06.3: 10.9% vs 9.9%), insomnia (R40.8: 6.7% vs 8.7%), dyspnea (R06.9: 11.4% vs 9.8%), overweight and obesity (E66: 14.0% vs 13.9%), ADHD (F90: 3.7% vs 8.7%), or major depressive disorders (F32-33: 7.7% vs 8.7%)

Pre-Narcopal Prescription Medications & Sleep Testing (Figure 1 and Table 2):
• Use of amphetamines and antidepressants were significantly lower in the NT2 compared to NT1 cohorts prior to diagnosis of narcolepsy.
• Bromocriptine and modafinil use were both higher in the NT2 cohort, however, only use of bromocriptine was significantly greater (24.7% vs. 8.7%, P<0.001).
• Nearly 40% of patients with NT2 underwent sleep testing prior to diagnosis compared to nearly 16% of those diagnosed with NT1, P=0.001

CONCLUSIONS

• This is one of a few studies to compare pediatric patients with and without cataplexy in a real-world setting and the only one known to use electronic medical records for analysis.
• A significant difference in the racial distribution of pediatric narcolepsy patients diagnosed with and without cataplexy was observed, but it is unknown if this difference remains in adult patients diagnosed with narcolepsy.
• While not all patients underwent sleep testing prior to their diagnosis, a greater proportion of those ultimately diagnosed without cataplexy had.
• Antidepressant treatment is not recommended in the absence of cataplexy, however a small proportion of patients did remain on treatment following their diagnosis.
• CNS stimulants and modafinil/amfodarol, not recommended in the presence of cataplexy, were both used for large proportions of these patients.

Table 1. Patient demographics

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>NT1 n = 299</th>
<th>NT2 n = 299</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>55.6%</td>
<td>42.1%</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>26.1%</td>
<td>42.8%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3.5%</td>
<td>1.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unknown</td>
<td>14.8%</td>
<td>13.6%</td>
<td></td>
</tr>
<tr>
<td><strong>Age at Diagnosis (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-9</td>
<td>28.1%</td>
<td>30.7%</td>
<td></td>
</tr>
<tr>
<td>≥10</td>
<td>36.5%</td>
<td>45.6%</td>
<td></td>
</tr>
<tr>
<td>15-17</td>
<td>20.8%</td>
<td>20.3%</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Pre-index sleep testing

<table>
<thead>
<tr>
<th>Test Type</th>
<th>NT1 n = 299</th>
<th>NT2 n = 299</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.1%</td>
<td>8.4%</td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>84%</td>
<td>15.8%</td>
<td></td>
</tr>
<tr>
<td><strong>Sodium Oxalate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11.3%</td>
<td>0.8%</td>
<td></td>
</tr>
<tr>
<td><strong>Sodium Oxalate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>20.9%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Modafinil/amfodarol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.7%</td>
<td>0.9%</td>
<td></td>
</tr>
<tr>
<td><strong>Modafinil/amfodarol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.0%</td>
<td>1.1%</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Pre-index medications

Figure 2. Odds of guideline recommended narcolepsy treatment (NT1 vs NT2)

• Post-index antidepressant [32.2% vs. 5.3%, P<0.001; OR 8.4 (4.4,15.9)] and sodium oxalate [6.7% vs. 3.2%, P=0.023; OR 2.7 (1.1, 6.8)] use was significantly greater in NT1 than NT2.
• Modafinil/amfodarol [17.4% vs. 18.4%] and CNS stimulants [44.2% vs. 41.8%] were similarly utilized in both cohorts, P=0.812 and P=0.639

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References:
3. Modafinil/amfodarol. This included stimulants. For comparison, the incidence for modafinil/amfodarol in our data was 17.4% (NT1) and 18.4% (NT2), with similar utilization in both cohorts.