

# Restless Legs Syndrome and Quality of Sleep in Type 2 Diabetes

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**OBJECTIVE** — To investigate the presence of restless legs syndrome (RLS) and the quality of sleep in a population of type 2 diabetic patients.

**RESEARCH DESIGN AND METHODS** — The study population was composed of 100 consecutive patients regularly attending a diabetes clinic at the University Hospital of the Federal University of Ceará. The subjects' quality of sleep was assessed by the Pittsburgh Sleep Quality Index, and excessive daytime sleepiness (EDS) was measured by the Epworth Sleepiness Scale. The RLS was diagnosed using the four minimum criteria defined by the International Restless Legs Syndrome Study Group. Other relevant clinical and laboratory parameters were obtained by interview and chart review.

**RESULTS** — RLS was found in 27% of patients. Poor sleep quality was present in 45% of cases and was associated with age ( $P = 0.04$ ), peripheral neuropathy ( $P = 0.001$ ), and RLS ( $P = 0.000$ ). EDS was found in 26% of patients. Logistic regression analysis revealed an association between RLS and peripheral neuropathy (odds ratio 12.85 [95% CI 2.83–58.40],  $P = 0.001$ ).

**CONCLUSIONS** — RLS is common in type 2 diabetic patients and can be a major cause of sleep disruption in these patients.

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**D**iabetes is a lifelong disease of increasing incidence in the Western world and is frequently comorbid with other disorders such as retinopathy, peripheral neuropathy, and nephropathy (1,2). Most patients develop diabetes after age 40 years, and, although much progress has been made in therapy, the majority of diabetic patients continue to die from macrovascular complications (i.e., cardiovascular disease) (3).

Recently it has become clear that sleep disturbances (e.g., chronic insomnia, sleep apnea) have a major impact on health and quality of life; this adverse impact can usually be reversed by adequate diagnosis and treatment (4). Neuropathy may also contribute to the significant reduction in quality of life for patients (5).

These problems are frequently overlooked on routine medical interviews; furthermore, in some cases, short-term disturbances of sleep may evolve into chronic conditions (6). The indiscriminate use of sleeping pills may further disrupt the sleep-wake cycle and contribute to stress in patients with sleep disorders (7). In type 2 diabetes, sleep disturbances are believed to be common (8) and have been attributed to impaired glucose metabolism and general physical distress (9).

Restless legs syndrome (RLS) is a common neurological condition characterized by unpleasant sensations deep inside the legs that occur at rest, especially at bedtime (10,11). The paresthesias are accompanied by an irresistible urge to move the limbs, with movement tempo-

rarily relieving the symptoms (12,13). RLS patients experience discomfort and complain of disturbances in initiating and maintaining sleep, sleepiness, and less-refreshing sleep (14). The intensity of sensory and motor symptoms can vary throughout a patient's lifetime but generally tends to increase with advancing age. RLS has been reported in association with various conditions, such as iron deficiency, rheumatoid arthritis, uremia, hypothyroidism, and polyneuropathy (15). There have also been reports of an association between RLS and diabetes (16), although this was not confirmed by some investigators (17). Because diabetes is a common cause of polyneuropathy, a higher prevalence of RLS should be expected in the subgroup of RLS patients who also have diabetes. More studies looking into the prevalence and risk factors for RLS among diabetic patients are currently needed.

In this study, we investigated the quality of sleep and the presence of RLS in a population of type 2 diabetic patients.

## RESEARCH DESIGN AND METHODS

For this study, 110 consecutive patients under age 70 years who had type 2 diabetes, regardless of disease duration, and regularly attended a diabetes outpatient clinic were initially recruited. Of those subjects, 10 were excluded because of poor health, low education level, or an unwillingness to participate. Financial compensation was not provided for any subject. The study protocol was approved by the local research ethics committee, and written informed consent was obtained in all cases.

This was a cross-sectional study of patients with a clinical diagnosis of type 2 diabetes. Demographic and clinical data were recorded using a closed-question data collection instrument. All patients were studied when they were in a stable clinical condition; specifically, they showed no presence of any infectious, traumatic, or other acute complications in the 3 months prior to the study, as assessed by their history and a review of their medical records. Neurological examinations, which included a search for peripheral neuropathy as described below, was performed by one of the investi-

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**Abbreviations:** EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index; RLS, restless legs syndrome.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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**Table 1—Demographic and clinical characteristics of study subjects**

n	100
Sex (male/female)	27/73
Age (years)	58.3 ± 12.3 (34–87)
Diabetes duration (years)	9.8 ± 7.6 (1–40)
BMI (kg/m <sup>2</sup> )	26.9 ± 4.7 (16.8–45.8)

Data are means ± SD (range).

gators. All variables were measured concurrently.

### Assessment procedures

RLS was established using the minimum criteria defined by the International Restless Legs Syndrome Study Group: 1) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; 2) the urge to move or the beginning or worsening of unpleasant sensations during periods of rest or inactivity, such as lying or sitting; 3) the urge to move or unpleasant sensations that are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues; and 4) the urge to move or unpleasant sensations that are worse in the evening or night than during the day or occur only in the evening or night (18).

Sleep quality was evaluated by the Pittsburgh Sleep Quality Index (PSQI). This scale has seven components, each one dealing with a major aspect of sleep: 1) subjective quality of sleep, 2) sleep onset latency, 3) sleep duration, 4) sleep efficiency, 5) the presence of sleep disturbances, 6) the use of hypnotic or sedative medication, and 7) the presence of daytime disturbances, as an indication of daytime alertness. Individuals with a PSQI score of six or more were considered poor sleepers (19).

Daytime somnolence was assessed by the Epworth Sleepiness Scale (ESS). This is a validated questionnaire containing eight items that measure a subject's expectation of dozing in eight hypothetical situations. Dozing probability ratings

**Table 2—Subjects' comorbid disorders**

n	100
Peripheral neuropathy	62
Hypertension	53
Dyslipidemia	38
Visual disorders	22
Acute myocardial infarction	7
Stroke	3

Data are percent.

**Table 3—Logistic regression analysis between poor quality sleep (PSQI score ≥6) and clinical and laboratory parameters**

	PSQI <6	PSQI ≥6	OR (95% CI)	P
n	55	45	—	—
Age (years)	55.9 ± 13.02	60.9 ± 11.1	1.03 (1.00–1.06)	0.04*
Sex (male/female)	16/39	11/34	0.84 (0.34–2.07)	0.70
Diabetes duration (years)	9.17 ± 7.93	10.72 ± 7.28	1.02 (0.97–1.08)	0.31
ESS score	6.53 ± 3.67	8.17 ± 5.12	1.09 (0.99–1.19)	0.07
RLS score	1.35 ± 2.51	3.88 ± 3.13	1.31 (1.15–1.56)	0.00*
Blood glucose (g/dl)	188.23 ± 66.23	176.78 ± 56.84	0.99 (0.99–1.00)	0.37
Peripheral neuropathy (present/absent)	27/28	37/8	0.21 (0.08–0.54)	0.001*

Data are means ± SD unless otherwise noted. P value is for comparison between patients with and without poor quality of sleep. \*P < 0.05.

range from zero (no probability) to three (high probability). An ESS score of 10 or more indicates excessive daytime sleepiness (EDS) (20).

Polyneuropathy was diagnosed clinically according to published criteria (21). A trained investigator assessed subjects' sensory function, distal muscle strength, and select reflexes. Distal sensory function was examined bilaterally using light touch, temperature, sharp (pin), and vibration sense. Distal muscle strength (finger spread, great toe extension, ankle dorsiflexion) and deep tendon reflexes (biceps brachii, quadriceps femoris, and Achilles) were also assessed bilaterally. Patients having a pain syndrome, other sensory complaints, and alterations in the neurological evaluation such as those consistent with symmetrical distal polyneuropathy were considered to have polyneuropathy.

Data on complete blood count, electrolyte levels, renal function, and medication in the last 30 days were obtained from medical records. BMI was calculated as the ratio between weight (in kilograms) and squared height (in meters).

### Statistical analysis

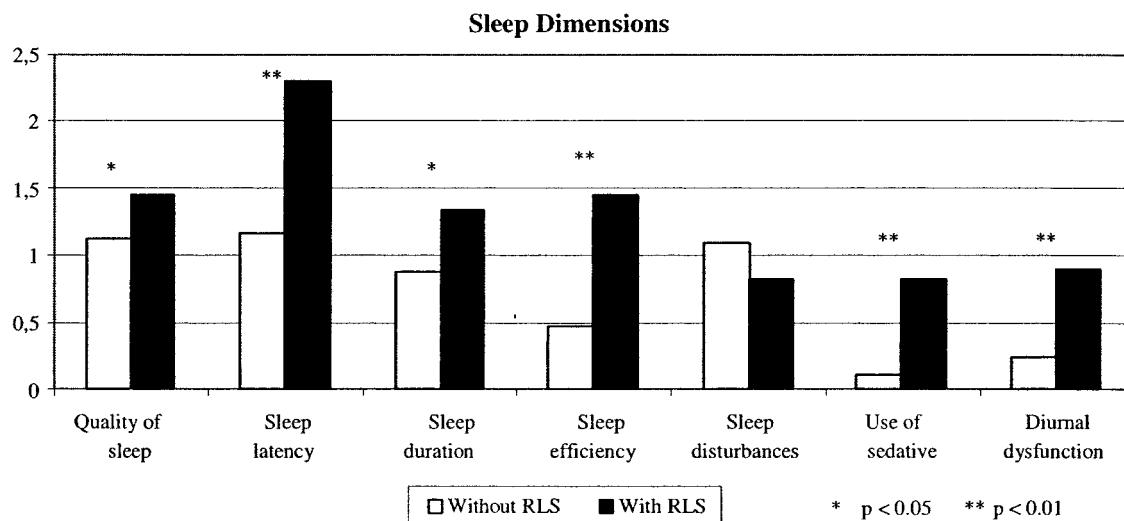
Data were analyzed using the Statistic Package for Social Sciences (Norusis, 1993) software. For statistical analysis and data description, patients were stratified according to the presence of EDS. They were also grouped as good or poor sleepers. Logistic regression was used to compare poor quality sleep, EDS, RLS, and other clinical parameters. ANOVA was used to compare PSQI measures from patients with and without RLS. Statistical significance was defined at 95% ( $P < 0.05$ ). Data are given as means ± SD.

**RESULTS**— Subject characteristics are given in Table 1. The common comorbidities were peripheral neuropathy (62%), arterial hypertension (53%), dyslipidemia (38%), and visual disorders (22%) (Table 2). Subjects with a BMI >25 were considered to be overweight ( $n = 33$ ) and those with a BMI >30 as obese ( $n = 9$ ).

Hemoglobin levels were  $12.86 \pm 1.34$  g/dl (range 8.5–13.8); anemia (hemoglobin level <12.0 g/dl) was present in 11% of cases. Cholesterol levels were  $221.2 \pm 53.0$  mg/dl (range 90–449). Creatinine levels were  $0.86 \pm 0.28$  mg/dl (range 0.4–2.0, except for one case who presented with a level of 5.3 mg/dl). HbA<sub>1c</sub> was  $7.7 \pm 1.9\%$  (range 3.1–11.8) in the 54 patients assessed. The most common medications used by subjects were oral antihyperglycemic medications (59%), antihypertensive drugs (54%), sedatives or analgesics (41%), insulin (32%), and statins (27%).

RLS was detected in 27 patients, 25 of whom had peripheral neuropathy. An association between RLS and peripheral neuropathy was confirmed by logistic regression analysis (odds ratio [OR] 12.85 [95% CI 2.83–58.40],  $P = 0.001$ ). Other factors did not contribute significantly to the presence of RLS.

Sleep quality was evaluated by the PSQI ( $n = 100$ ; mean PSQI score  $6.29 \pm 3.84$ ). Poor sleep quality (PSQI ≥6) was present in 45% of the subjects and was related to age, presence of RLS, and peripheral neuropathy (Table 3). Subjects with RLS showed poorer general quality of sleep ( $P = 0.02$ ), longer sleep latency ( $P = 0.000$ ), shorter sleep duration ( $P = 0.04$ ), less sleep efficiency ( $P = 0.000$ ), more use of sedatives ( $P = 0.000$ ), and



**Figure 1**—Study subjects' quality of sleep components (sleep dimensions) as assessed by the PSQI. Type 2 diabetic patients with RLS (n = 27) showed significant impairment (except for sleep disturbances) compared with diabetic subjects without RLS (n = 73).

more diurnal dysfunction ( $P = 0.000$ ) on the PSQI evaluation (Fig. 1). EDS was found in 26% of cases and was not related to the presence of RLS (OR 1.06 [95% CI 0.92–1.22],  $P = 0.40$ ).

**CONCLUSIONS**— This study showed that RLS is common in patients with type 2 diabetes and is associated with peripheral neuropathy and poor quality sleep.

Epidemiological surveys have usually shown a prevalence of RLS ranging from 5 to 15% in the general population (22,23). The incidence has been reported to be higher in female subjects and to increase with age (23). Previously, in a study with fewer cases than this study, the prevalence rate of RLS in type 2 diabetic subjects was not found to differ significantly from that in control subjects (24.1 vs. 12.5%) (17). A recent study found only one case of RLS among 46 children and adolescents with type 1 (insulin-dependent) diabetes (24).

A large proportion of our subjects reported having poor quality sleep. This finding was consistent with previous studies in diabetic patients (6,9,17). We found that poor sleep was significantly correlated with the presence of RLS and polyneuropathy. There was also a correlation between older age and poor sleep. Although sleep complaints are more frequent in older subjects (23), in our study these complaints could also have been related to increasing severity of RLS. It should be noted that patients do not always report poor quality sleep to their physicians. Significant changes in sleep may not result in sleep complaints, sug-

gesting that many individuals adapt their perception of what is acceptable sleep.

Our data confirmed that EDS is common in adult diabetic patients. EDS can be related to multiple causes, including circadian rhythm and mood disorders, use of sedatives, RLS, and sleep-disordered breathing. Because our study was not specifically designed to differentiate among different causes of daytime somnolence, the reasons for this finding are not immediately clear.

RLS is a disabling and uncomfortable process that may interfere with falling asleep and lead to sleep deficit. Treatment with dopaminergic agents, opioids, benzodiazepines, and anticonvulsant drugs (e.g., topiramate) have been reported to improve somatic complaints and sleep parameters (15,23,25). A number of RLS patients also have periodic limb movements during sleep, defined as stereotyped, periodic, jerking movements, typically consisting of flexion of the ankle, knee, or hip. Periodic limb movements are sometimes accompanied by arousals from sleep, leading to sleep fragmentation and EDS. A periodic limb movement index (i.e., number of periodic limb movements per hour of sleep) greater than five for the entire night on a full polysomnography is required for the diagnosis of periodic limb movement disorder (14). The choice of a specific therapy for this disorder is controversial as periodic limb movement disorder may not be harmful to sleep quality and can be associated with other sleep disorders, such as sleep apnea.

In summary, RLS is frequently found in type 2 diabetic patients and can lead to

poor sleep quality in these patients. An active search for the presence of RLS is warranted, particularly in subjects with polyneuropathy.

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