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Brief Communication

# Excessive daytime somnolence is associated with hypoglycemia in adult Latinos with type 2 diabetes mellitus

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ABSTRACT

*Objective:* This study aimed to determine the frequency of sleep disorders in hypoglycemic diabetic patients and possible relationships with scores of sleep disorders and restless legs syndrome in mestizo population in Guayaquil, Ecuador.
*Methods:* A multicenter, cross-sectional study conducted at an outpatient endocrinology clinic in urban and rural Ecuador regions, included 290 participants with type 2 diabetes mellitus with severe hypoglycemic episodes, completed, validated, and culturally adapted sleep questionnaires to assess daytime sleepiness, risk of sleep apnea and restless legs syndrome. Logistic regression analysis was conducted to identify factors associated with severe hypoglycemia.
*Results:* The prevalence of EDS was 56.8%, RLS prevalence of 46.2%, and 38.6% prevalence of high risk Berlin score. Multivariate logistic regression indicated hypoglycemic T2DM in the range of 56–75 years old were more likely to have high ESS (p 0.0001).
*Conclusion:* A high prevalence of sleep disorders in diabetic Latinos living in Ecuador was evidenced. The presence of somnolence in patients older than 56 years and high HbA1c levels should alert the clinician for the occurrence of hypoglycemic episodes.



## 1. Introduction

Sleep disorders are associated with components of the metabolic syndrome and type 2 diabetes mellitus (T2DM2). Among sleep disorders, excessive daytime sleepiness (EDS) is a cause of accidents, cognitive impairment, and reduced work efficiency. Increasing attention has been paid to the connection between diabetes and EDS [1,2].

EDS has proven to be a predictor of severe hypoglycemia in T2DM [2]. Hypoglycemia is documented by Whipple's triad: symptoms consistent with hypoglycemia, low plasma glucose concentration and relief of those symptoms when the plasma glucose concentration is raised. In people with T2DM, hypoglycemia can be classified as asymptomatic or severe, which requires the assistance of another individual. These symptoms include, but are not limited to, palpitations, tremor, hunger, and sweating. Hypoglycemia is a known adverse side effect of insulin and sulfonylurea treatment in T2DM [3].

There are several factors influencing the risk of severe hypoglycemia including duration of insulin treatment, older age, comorbidities, and renal impairment. Sleep disorders are also very common among patients with T2DM including obstructive sleep apnea, insomnia, and excessive daytime sleepiness. Breathing-related sleep disorders are associated with daytime somnolence in up to 75% of people with T2DM [1,2].

Obstructive sleep apnea (OSA) is a well-recognized factor associated with T2DM and a cause of excessive daytime sleepiness, with a prevalence of 37.2% in diabetic patients with Hemoglobin A1c (HbA1c) > 7% [4,5].

Another sleep disorder that may affect the management of diabetes but is not well recognized as a significant contributor to T2DM health outcomes, is restless legs syndrome (RLS). RLS is a sleep disorder that causes an irresistible urge to move the legs at night. This urge is accompanied by paresthesias in the legs. The

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association between RLS and diabetes has not been studied carefully, and the effects of RLS on T2DM are not well known [4,6–8].

Despite the recognition of sleepiness as a major public health issue, its clinical associated factors and pathogenesis have not been entirely clarified. Previous studies have shown that patients with T2DM with increased daytime sleepiness measured by Epworth Sleepiness Scale (ESS) and Berlin questionnaire are more likely to experience severe hypoglycemia [1,2].

Increased hypoglycemic episodes relate to EDS, but there is no data available about the relationship between hypoglycemia and restless leg syndrome [2].

The objective of the study was to determine the association between hypoglycemic episodes with excessive daytime sleepiness and specific sleep disorders in a Latino mestizo population in Ecuador.

## 2. Methods

### 2.1. Study settings and guidelines

Participants (n: 290) were selected from the outpatient Endocrinology clinic at Luis Vernaza Hospital, Guayaquil and outpatient rural area from Paccha, Azuay. Approval of the institutional ethics committee from Luis Vernaza Hospital was received (Protocol HLV-DOF-CCI-003) and informed consent was obtained to gather data from patients with T2DM and recollect information about their sleep. After consent was obtained and self-administered, questionnaires were completed.

### 2.2. Subjects and study design

Patients were selected under the criteria of: T2DM with at least one-year diagnosis who were on treatment with insulin or oral antidiabetic drugs and have had at least one severe hypoglycemic episode. Exclusion criteria: end stage renal disease, treatment with beta blockers, and incomplete records or diagnosis of neoplasia. Of 323 patients evaluated, 290 met the inclusion criteria and 33 patients were excluded: 12 with incomplete records, seven end stage renal disease, 14 were unable to fill the questionnaire.

Participants completed the validated Spanish versions of Epworth Sleepiness Scale (ESS) [9], Berlin questionnaire [10] and four minimal diagnostic criteria for restless legs syndrome [11] to assess daytime sleepiness, risk of sleep apnea, and clinical diagnosis of RLS, respectively. History of severe hypoglycemia was documented from the question: Have you ever had an episode of low blood glucose when you have needed someone else to treat you? All patients were recruited in a four-month period and were aged 35–91 years from Guayas and Azuay region [9–11].

High risk Berlin score was defined if two out of three categories were present (categories were snoring, sleepiness, and either self-reported hypertension or BMI >30 kg/m$^2$). The ESS was considered high if the score was ≥11.

At the Endocrinology clinic, attending physicians identified eligible patients and send them to the supervisor of the study in order to get the informed consent. After obtaining consent each patient completed the three questionnaires from ESS, Berlin, and RLS (Annex 1). The questions were selected to get information concerning: daytime sleepiness, risk of sleep apnea, and symptoms of RLS.

Data obtained during the Endocrinology clinic visit included: age in years, gender, age at diagnosis of T2DM, type of treatment including oral medication, insulin or both, body mass index, and HbA1c (Table 1).

**Table 1**
Features of T2DM patients from Guayaquil and Paccha, Ecuador.

| | n = 290 | % |
|---|---|---|
| ***Sociodemographic characteristics*** | | |
| **Gender** | | |
| Female | 207 | 71.30% |
| Male | 83 | 28.60% |
| **Age** | | |
| 35–55 years | 73 | 25.17% |
| 56–75 years | 158 | 54.48% |
| 76–95 years | 59 | 20.34% |
| ***Clinical characteristics*** | | |
| **BMI** | | |
| Ideal weight (18.5–25) | 93 | 32.06% |
| Overweight (25.1–30) | 140 | 48.27% |
| Obesity (>30) | 57 | 19.65% |
| **HbA1c** | | |
| Less than 7% | 95 | 32.75% |
| More than 7% | 195 | 67.24% |
| **Time with T2DM diagnosis** | | |
| 1–5 years | 123 | 42.41% |
| 5–10 years | 101 | 34.82% |
| >10 years | 66 | 22.75% |
| **Treatment** | | |
| Oral antidiabetic | 212 | 73.10% |
| Insulin | 47 | 16.20% |
| Oral antidiabetic and Insulin | 31 | 10.68% |
| ***Sleeping characteristics*** | | |
| **Epworth Sleepiness scale** | | |
| <11 | 125 | 43.10% |
| >11 | 165 | 56.89% |
| **Restless leg syndrome** | | |
| Yes | 134 | 46.20% |
| No | 156 | 53.79% |
| **Berlin Score** | | |
| High risk | 112 | 38.62% |
| Low risk | 178 | 61.37% |

### 2.3. Sample size

A sample size of 355 patients was obtained by statistics parameters based on the following assumption: an expected prevalence of hypoglycemia of 50% probability among patients with diabetes, a 5% type 1 error, a power of 80%, a confidence interval of 95%.

## 3. Statistical analysis

Statistical analysis was performed using STATA software version 14.1 for Mac and Excel for Mac 2016 with an alpha set to 5%. Basic descriptive statistics were used to calculate mean and standard deviation of quantitative variables such as age, BMI, HbA1c, years with T2DM. Qualitative categorical variables such as gender, type of treatment, ESS score, Berlin score, and RLS questionnaire are reported as frequencies and percentages (Table 1). Qualitative and quantitative variables were compared using Chi square and Fisher test to determine associations of demographic, clinical, and sleeping variables with high ESS (≥11). For ordinal qualitative variables Kruskal–Wallis was obtained to correlate the variables with sleeping questionnaires.

The prevalence of severe hypoglycemia was compared in those with high and low risk Berlin, ESS score and presence or absence of RLS criteria using Pearson $X^2$. Logistic regression was performed to evaluate the impact of ESS, Berlin score, presence of RLS, age, sex, duration of diabetes, hemoglobin A1c (HbA1c), BMI and treatment type on probability of severe hypoglycemia. Logistic regression was completed to discern the best predictors of severe hypoglycemia. Data were analyzed using IBM SPSS Statistics version 22 Guayaquil, Ecuador.