



**HAL**  
open science

## Screening for sleep-disordered breathing in people with type 1 diabetes by combining polysomnography with glucose variability assessment

Damien Basille, Marine Timmerman, Aurelie Basille-Fantinato, Abdallah Al-Salameh, Salha Fendri, Jean-Daniel Lalau

► **To cite this version:**

Damien Basille, Marine Timmerman, Aurelie Basille-Fantinato, Abdallah Al-Salameh, Salha Fendri, et al.. Screening for sleep-disordered breathing in people with type 1 diabetes by combining polysomnography with glucose variability assessment. *Diabetes Research and Clinical Practice*, 2022, 185, 10.1016/j.diabres.2022.109786 . hal-03732940

**HAL Id: hal-03732940**

**<https://u-picardie.hal.science/hal-03732940>**

Submitted on 22 Jul 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

**Screening for sleep-disordered breathing in people with type 1 diabetes by combining polysomnography with glucose variability assessment.**

**Running head: sleep-disordered breathing in type 1 diabetes**

Damien Basille<sup>1-2\*</sup>, Marine Timmerman<sup>3\*</sup>, Aurélie Basille-Fantinato<sup>4</sup>, Abdallah Al-Salameh<sup>3-5</sup>, Salha Fendri<sup>3</sup> and Jean-Daniel Lalau<sup>3,5</sup>,

From:

<sup>1</sup> Department of Pneumology, Amiens University Hospital, Amiens, France.

<sup>2</sup> AGIR Unit, University Picardie Jules Verne, 80054, Amiens Cedex, France.

<sup>3</sup> Department of Endocrinology-Diabetes Mellitus-Nutrition, Amiens University Hospital, Amiens, France.

<sup>4</sup> Sleep and Vigilance Disorder Unit, Amiens University Hospital, Amiens, France.

<sup>5</sup> PériTox, UMR-I 01, University of Picardie Jules Verne, Amiens, France.

\* DB and MT contributed equally to this article and should both be considered as first authors.

**Correspondence to:**

Jean-Daniel Lalau (Lalau.Jean-Daniel@chu-amiens.fr)

Service d'Endocrinologie, Diabétologie et Nutrition, Hôpital Nord, CHU Amiens-Picardie, Amiens 80054 Cedex 01, France.

Tel: +33-322-455-895

Fax: +33-322-455-334

**Word count:** 2562 words

**Abstract:** 199 words

**Tables:** 3

**Figures:** 1

**References:** 24

**Supplemental material:** none.

## HIGHLIGHTS

- Sleep disorders (SDB) were studied in adults with type 1 diabetes
- Polysomnography and glucose variability assessment were combined to screen for SDB
- SDB was highly prevalent and associated with obesity
- Sleep disorders were not associated with glucose variability or low glucose values

## ABSTRACT

**Aims:** There are few published data on sleep-disordered breathing (SDB) in type 1 diabetes (T1DM). Here, we used a combination of polysomnography and glucose variability assessment to screen for SDB.

**Methods:** In a prospective, single-centre study, adults with T1DM underwent polysomnography and continuous glucose monitoring during a single night. We measured high glucose variability and the occurrence of a low or very low glucose level. Mild and moderate-to-severe SDB were defined as an apnoea-hypopnoea index above 5/h and 15/h, respectively.

**Results:** We studied 46 patients (25 men; median age: 42 [35-54]; diabetes duration: 18 years [13-29]; body mass index (BMI): 24.8 kg/m<sup>2</sup> [23.0-28.9]). SDB was present in 17 patients (37.0%) overall (mild SDB: n=9; moderate-to-severe SDB; n=8). When compared with the absence of SDB or mild SDB, moderate-to-severe SDB was associated with a higher BMI (29.8 kg/m<sup>2</sup> [27.8-31.1]) and a longer diabetes duration (26 years [18-31]) but not with above-target glucose variability or more sleep disorder symptoms. Conversely, sleep disorder symptoms were not more frequent in patients with above-target glucose variability.

**Conclusion:** SDB was highly prevalent and associated with obesity. According to the methods used here, sleep disorders were not associated with above-target glucose variability or low glucose values.

**Keywords:** sleep-disordered breathing; type 1 diabetes; polysomnography; continuous glucose monitoring; glucose variability.

## **Introduction**

Screening for sleep-disordered breathing (SDB) should be a public health objective *per se* because this highly prevalent, often insidious (and therefore underdiagnosed) disorder is strongly associated with non-fatal and fatal cardiovascular events (1). Obesity is the primary risk factor for SDB (2,3). Hence, it is not surprising that the prevalence of SDB is strongly linked to type 2 diabetes mellitus (T2DM) (4,5) and metabolic syndrome (6). SDB and T2DM form a vicious circle; obesity, high insulin levels and insulin resistance are associated with sleep disorders (7), whereas sleep disorders are associated with incident T2DM (4,5).

In view of the known link to T2DM, we decided to study the prevalence of SDB in people with type 1 diabetes mellitus (T1DM). Firstly, T1DM (with the complete absence of insulin) generally occurs in non-obese people. Secondly, autonomic neuropathy is a frequent complication of T1DM and increases the risk of developing SDB (8–11). Thirdly, the presence of SDB might (at least in theory) exacerbate the characteristic glucose variability seen in T1DM; even in healthy people, hypoxemia and sleep fragmentation are associated with decreased insulin sensitivity, elevated sympathetic tone, and elevated plasma glucose levels (5). Hence, SDB might further increase the risk of diabetic vascular complications in people with T1DM.

There are few published reports on the association between T1DM and sleep disorders. Although SDB appears to be more prevalent in people with T1DM than in the general population (5), the true extent of this disorder has not been unambiguously determined. In fact, the definition of SDB and the methods used to determine the presence and severity of this condition (questionnaires, nasal airflow, snoring, actimetry, oximetry, polygraphy, polysomnography, etc.) varied markedly from one study to another (12–16). Lastly, the relationship between sleep characteristics and glucose variability in adults with T1DM has not previously been investigated (17).

To this end, we used a combination of polysomnography and glucose variability measurements to assess SDB in adults with T1DM.

## **Patients and methods**

### **Study design**

We performed a cross-sectional, single-centre clinical study of PSG coupled to glucose variability assessment. Given that the treatment of SDB depends on its severity, we distinguished between mild or absent SDB on one hand and moderate-to-severe SDB on the other. We then compared these two groups with regard to their demographic characteristics. Furthermore, we compared the prevalence of moderate-to-severe SDB in our study population vs. that observed in the general population. Lastly, we assessed the sleep characteristics as a function of the presence or absence of abnormal glucose variability and hypoglycaemic episodes.

The study was sponsored by Amiens University Hospital (Amiens, France) and was conducted in accordance with the Declaration of Helsinki, good clinical practice guidelines, and the French

legislation on clinical research and data protection. Moreover, the study's objectives and procedures were approved by an independent ethics committee at Clermont-Ferrand University (Clermont-Ferrand, France; reference: 2017-A02250-53). All the included patients gave their written, informed consent to participation.

### Participants

We included consecutive, scheduled day patients admitted to the Department of Endocrinology-Diabetology-Nutrition at Amiens University Hospital (Amiens, France) for poor diabetes control, the intensification of insulin therapy or the initiation of insulin pump therapy between November 2017 and January 2019 and who had given their consent to participation in the study soon after admission.

The inclusion criteria were as follows: age 18 or over, T1DM diagnosed at least 3 years previously, and autoantibodies against glutamic acid decarboxylase, insulinoma-associated antigen 2 and/or insulin.

The exclusion criteria were as follows: T2DM; poor treatment adherence (failure to attend follow-up consultations, no adherence to glucose self-monitoring etc.), physician-diagnosed sleep disorders, continuous positive airway pressure treatment; facial anomalies compatible with acromegaly; neuromuscular diseases (e.g. Steinert's disease), and non-standard work hours (e.g. shift work or night work), and legal guardianship.

### Data on T1DM

Diabetic complications were defined as (i) nephropathy (evidenced by microalbuminuria (30-300 mg per day) or proteinuria (>300 mg/day) in patients with and without renal failure (calculated using the CKD-EPI formula); (ii) retinopathy (evidenced by a recent funduscopy examination or retinography); (iii) sensorimotor polyneuropathy (clinical symptoms and a positive monofilament test) or autonomic neuropathy (blood pressure and heart rate changes after standing, or a prolonged QT interval on an ECG); and (iv) macroangiopathy (a history of cardiovascular events and large vessel stenosis on Doppler ultrasound).

All clinical and laboratory data were determined during the hospital stay shortly before study entry.

### Comparisons of the prevalence of SDB

We used Peppard et al.'s community-based study (18) in the United States as a reference for the prevalence of SDB in the general population, although the data covered the periods 1988-1994 and 2007-2010 only. In brief, Peppard et al. estimated the prevalence of SDB in the state of Wisconsin by analyzing data on participants selected at random from a population of adults in employment. A total of 1,520 participants (aged 30-70) underwent baseline polysomnography studies. The prevalence of sleep-disordered breathing was then modelled as a function of age,

sex, and body mass index (BMI), and estimates were extrapolated to the US BMI distributions estimated in the National Health and Nutrition Examination Survey. The latest prevalence estimates [95% confidence interval] for moderate-to-severe SDB were 10% [7–12] among men aged 30 to 49, 17% [15–21] among men aged 50 to 70, 3% [2–4] among women aged 30 to 49, and 9% [7–11] among women aged 50 to 70.

Of course, these estimates might need to be updated because of the increase in the prevalence of obesity over the last decade. In France, the prevalence of obesity is lower than that in the US but has increased progressively over the last 20 years (19).

### Procedures

Patients were admitted for standard PSG (from 7pm to 8am) using the Brainnet System (Medatec, Brussels, Belgium) coupled to an electroencephalogram, an electrooculogram, an electromyogram, continuous nasal airflow monitoring, thoracic and abdominal movement (using strain gauges) and oxygen saturation measurement with a pulse oximeter (Medatec). Continuous glucose monitoring (CGM) during the night was performed with the G4 Platinum subcutaneous sensor system (Dexcom, San Diego, CA, USA) and the Vibe monitor (Animas Corporation, Chesterbrook, PA, USA). Prior to PSG, excessive daytime sleepiness was scored on the Epworth sleepiness scale; a score of 11 or more was considered to be positive.

### Polysomnography

Obstructive apnoea, central apnoea, mixed apnoea and hypopnea were defined according to the 2014 American Academy of Sleep Medicine standards (20). According to rule 1A, hypopnea was scored if all the following criteria were met: (i) the peak nasal pressure signal excursion dropped by  $\geq 30\%$ , relative to the pre-event baseline; (ii) the  $\geq 30\%$  drop in signal excursion lasted for at least 10 seconds; and (iii) the fall in oxygen desaturation was at least 3% (relative to the pre-event baseline) and/or was associated with arousal.

SDB was defined as an apnoea-hypopnoea index (AHI) of at least 5/h. The severity was defined as mild (AHI = 5–14/h), moderate (AHI = 15–29/h) or severe (AHI  $\geq 30$ /h) (21). All the polysomnography data were interpreted by the same trained neurophysiologist.

### Glucose variability and hypoglycaemic episodes

Above-target glucose variability during CGM was defined as a percentage coefficient of variation (%CV-CGM  $>36\%$ ) (22). Hypoglycaemia was classified as moderate ( $<70$  mg/dl) or severe ( $<54$  mg/dl) (23). All the CGM data were interpreted by the same trained diabetologist.

### Statistical analysis

We first tabulated the patients' baseline characteristics. In view of the data's non-normal distribution, continuous variables were expressed as the median [interquartile range (IQR)]. Categorical variables were expressed as the frequency (percentage).

We calculated the expected prevalence of moderate-to-severe SDB in our study cohort by using Peppard et al.'s sex, age and BMI distribution data (18). We compared this expected prevalence with the observed prevalence by applying a binomial test. In a sensitivity analysis, we considered a 30% increase in the expected prevalence. Group values were compared in Fisher's exact test or a non-parametric Mann-Whitney test, as appropriate. We assessed the correlations between the AHI on one hand and various anthropometric parameters (BMI, waist circumference, and neck circumference) and the %CV-CGM on the other by calculating Spearman's coefficient (separately for men and for women). Statistical analysis was performed with PASW Statistics 17 software (SPSS, Inc; Chicago, IL). All tests were two-tailed, and the threshold for statistical significance was set to  $p < 0.05$ .

## Results

Characteristics of the study population and the prevalence of SDB

Fifty-nine eligible patients were screened for inclusion during the study period. Of these, 46 met all the inclusion criteria and agreed to participate in the study. The patients' demographic characteristics are summarized in **Table 1**. The male/female sex ratio was 1.19:1, the median [IQR] age was 42 [35-54], and the median diabetes duration was 18 years [13-29]. The median BMI (24.8 kg/m<sup>2</sup> [23.0-28.9]) was close to the threshold for overweight; around one third of the patients were overweight, and one sixth were obese. Two-thirds of the patients were being treated with an insulin pump. For the study population as a whole, microvascular and neurological complications were more frequent than macrovascular complications (data not shown).

According to our screening technique, 17 patients (37.0%) had SDB; the disorder was mild in 9 patients (19.6%), moderate in 5 (10.9%), and severe in 3 (6.5%). Hence, there were 38 patients (82.6%) in the "absent/mild SDB" group and 8 (17.4%) in the "moderate-to-severe SDB" group. It should be noted that none of the female participants had moderate-to-severe SDB.

According to Peppard et al.'s models, the estimated prevalence of moderate or severe SDB in the general population (adjusted for age and sex) was 4.6%; the significantly greater value in our study population (17.4%,  $p = 0.001$ ) cannot be explained solely by the increase in the prevalence of obesity observed over the last 20 years (i.e. the time difference between Peppard et al.'s study and the present study) (**Figure 1**).

Glucose variability and hypoglycaemic episodes

The overnight CGM revealed that 22 participants (47.8%) had above-target glucose variability (%CV-CGM > 36%). One or more episodes of moderate hypoglycaemia (< 70 mg/dl) or severe

hypoglycaemia (<54 mg/dl) were observed in 19 (41.3%) and 13 (28.3%) participants, respectively (**Tables 2-3**). The sleep characteristics did not differ significantly as a function of the presence or absence of glucose variability or the presence or absence of hypoglycaemic episodes.

#### Correlation studies

We observed a statistically significant, positive correlation between the AHI on one hand and the BMI and waist and neck circumferences on the other in male patients but not in female patients (Table 4). The AHI was not correlated with %CV-CGM.

#### Discussion

The present prospective study is the first to have concomitantly assessed the prevalence of SDB and glucose variability in adults with T1DM. According to the literature, the prevalence of SDB in T1DM ranges from 46.3% (in a PSG study of 67 patients) (24) to 56.5% (in a polygraphy study of 23 patients) (14). The estimated prevalence of moderate-to-severe SDB ranges from 10.3% (in an airflow/pulse oximetry study of 58 patients) (13) to 23.1% (in a polygraphy study of 58 patients) (14). Our study results (a prevalence of 37% for SDB and 17.4% for moderate-to-severe SDB) are in line with these literature data. All the patients with moderate-to-severe SDB in our study were men. Only one study reported a sex difference in the prevalence of SDB in a univariable analysis, although this difference disappeared in a multivariable analysis (16). The other above-mentioned studies did not find a sex difference in the prevalence of SDB. However, these studies featured small population sizes.

The prevalence of SDB in T1DM therefore appears to be higher than that encountered in the general population, according to Peppard et al. Using baseline polysomnography data from 1520 adults (aged 30–70), the latter researchers estimated the prevalence of SDB for the period 1988–2011 (18).

The patients in our “moderate-to-severe SDB” and “no/mild SDB” groups did not differ significantly with regard to diabetes control (HbA1c) or above-target glucose variability. Other studies of SDB in people with T1DM did not find clinical or demographic differences as a function of the severity of SDB; however, none of these studies looked at glucose variability. It is noteworthy that in people with T2DM, severe SDB is associated with a higher HbA1c level (0.5%-0.8%).

Our data raise the question of the role of adiposity in SDB among people with T1DM. In the present study, patients with moderate-to-severe SDB had significantly higher BMI, waist circumference and neck circumference values -suggesting that greater adiposity is involved in the pathogenesis of SDB in this population. This hypothesis is supported by the facts that we observed moderate-to-severe SDB in men, in whom markers of adiposity were positively correlated with the AHI (in contrast to female patients). In contrast, AHI was not correlated with glucose variability (%CV-CGM). In other words, our present results do not support a hypothetical link between SDB



and T1DM (expressed as glucose variability, hypoglycaemic episodes, and/or autonomic neuropathy) per se.

It is noteworthy that (i) the patients with moderate-to-severe SDB did not have a greater frequency of clinical symptoms (which might contribute to the underdiagnosis of this condition) or a higher frequency of glucose variability or hypoglycaemic episodes, and (ii) sleep abnormalities were not more frequent in patients with marked glucose variability or frequent hypoglycaemic episodes.

The present study had a number of limitations. Firstly, we did not perform a multivariate analysis of the link between obesity and SDB. This search for other risk factors of SDB would have been interesting but was prevented by the fact that all the cases of moderate-to-severe SDB occurred in men. Secondly, given the small number of patients with diabetic complications, we did not take account of the possible association between the latter and SDB; any comparisons would have lacked statistical power. Thirdly, we did not take account of the number and duration of hypoglycaemic episodes. Fourthly, only two thirds of the patients were screened for autonomic neuropathy - a good candidate SDB risk factor. Lastly and most importantly (given the prevalence of overweight and obesity in our patients), our study lacked a control group of non-diabetic participants matched for body weight (although it is very difficult to constitute a control group matched for the main demographic characteristics).

Nevertheless, the study also had a number of strengths. Firstly, our study population (n=46) was relatively large. Secondly, we used the “gold standard” method (PSG) to assess SDB. Lastly, the present study is the only one to have recorded sleep and CGM data concomitantly in people with T1DM.

## **Conclusion**

According to the methods used in the present study, (i) the prevalence of SDB in T1DM was much higher than a literature value for the general population; (ii) moderate-to-severe SDB was observed only in male patients, in whom markers of adiposity were positively correlated with the AHI (in contrast to female patients); (iii) the patients having moderate-to-severe SDB were not more symptomatic and did not show more glucose variability or hypoglycaemic episodes; (iv) the prevalences of above-target glucose variability and hypoglycaemic episodes were not associated with a greater prevalence of sleep abnormalities, and (v) the low frequency of symptoms in the patients with SDB might contribute to the underdiagnosis of this condition.

Our results ultimately suggest that the high prevalence of SDB in patients with T1DM was linked to adiposity and not the diabetic state per se. We therefore suggest that all patients with T1DM and BMI  $\geq 30$  kg/m<sup>2</sup> and/or waist circumference  $\geq 100$  cm should be screened for SDB.

## **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### **Acknowledgements**

We are grateful to Homeperf (Amiens, France) for providing the Dexcom G4® Platinum sensors.

### **Authors Contributions**

Concept and design: MT and SF.

Full access to all of the data and responsibility for the integrity of the data and the accuracy of the data analysis: MT, DB, ABF and SF.

Acquisition, analysis, or interpretation of data: all co-authors.

Statistical analysis: DB.

Drafting the manuscript: MT, DB, AAS, SF and JDL.

Critical revision of the manuscript: all co-authors.

### **Funding**

None.

## References

1. Marin JM, Carrizo SJ, Vicente E, Agusti AGN. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet*. 2005;365(9464):1046-53.
2. Punjabi NM. The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;5(2):136-43.
3. Veasey SC, Rosen IM. Obstructive Sleep Apnea in Adults. *N Engl J Med*. 2019;380(15):1442-9.
4. Heffner JE, Rozenfeld Y, Kai M, Stephens EA, Brown LK. Prevalence of diagnosed sleep apnea among patients with type 2 diabetes in primary care. *Chest*. 2012;141(6):1414-21.
5. Reutrakul S, Mokhlesi B. Obstructive Sleep Apnea and Diabetes: A State of the Art Review. *Chest*. 2017;152(5):1070-86.
6. Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G. Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. *J Am Coll Cardiol*. 2013;62(7):569-76.
7. Balkau B, Vol S, Loko S, Andriamboavonjy T, Lantieri O, Gusto G, et al. High baseline insulin levels associated with 6-year incident observed sleep apnea. *Diabetes Care*. 2010;33(5):1044-9.
8. Bottini P, Redolfi S, Dottorini ML, Tantucci C. Autonomic neuropathy increases the risk of obstructive sleep apnea in obese diabetics. *Respir Int Rev Thorac Dis*. 2008;75(3):265-71.
9. Moțățăianu A, Maier S, Bajko Z, Voidazan S, Bălașa R, Stoian A. Cardiac autonomic neuropathy in type 1 and type 2 diabetes patients. *BMC Neurol*. 2018;18(1):126.
10. Meyer L, Massuyeau M, Canel C, Bahougne T, Assemi P, Perrin A-E, et al. Association of sleep apnoea syndrome and autonomic neuropathy in type 1 diabetes. *Diabetes Metab*. 2019;45(2):206-9.
11. Janovsky CCPS, Rolim LC de SP, de Sá JR, Poyares D, Tufik S, Silva AB, et al. Cardiovascular autonomic neuropathy contributes to sleep apnea in young and lean type 1 diabetes mellitus patients. *Front Endocrinol*. 2014;5:119.
12. Borel A-L, Benhamou P-Y, Baguet J-P, Halimi S, Levy P, Mallion J-M, et al. High prevalence of obstructive sleep apnoea syndrome in a Type 1 diabetic adult population: a pilot study. *Diabet Med J Br Diabet Assoc*. 2010;27(11):1328-9.
13. Schober A-K, Neurath MF, Harsch IA. Prevalence of sleep apnoea in diabetic patients. *Clin Respir J*. 2011;5(3):165-72.
14. Vale J, Manuel P, Oliveira E, Oliveira AR, Silva E, Melo V, et al. Obstructive sleep apnea and diabetes mellitus. *Rev Port Pneumol*. 2015;21(2):55-60.
15. Reutrakul S, Thakkestian A, Anothaisintawee T, Chontong S, Borel A-L, Perfect MM, et al. Sleep characteristics in type 1 diabetes and associations with glycemic control: systematic review and meta-analysis. *Sleep Med*. 2016;23:26-45.

16. Banghøj AM, Nerild HH, Kristensen PL, Pedersen-Bjergaard U, Fleischer J, Jensen AEK, et al. Obstructive sleep apnoea is frequent in patients with type 1 diabetes. *J Diabetes Complications*. 2017;31(1):156-61.
17. Perfect MM, Patel PG, Scott RE, Wheeler MD, Patel C, Griffin K, et al. Sleep, glucose, and daytime functioning in youth with type 1 diabetes. *Sleep*. 2012;35(1):81-8.
18. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177(9):1006-14.
19. Diouf I, Charles MA, Ducimetière P, Basdevant A, Eschwege E, Heude B. Evolution of obesity prevalence in France: an age-period-cohort analysis. *Epidemiol Camb Mass*. 2010;21(3):360-5.
20. The AASM Manual for the Scoring of Sleep and Associated Events: Summary of Updates in Version 2.1 [Internet]. The American Academy of Sleep Medicine; 2014 juill. Disponible sur: <https://j2vjt3dnbra3ps7ll1clb4q2-wpengine.netdna-ssl.com/wp-content/uploads/2017/11/Summary-of-Updates-in-v2.1-FINAL.pdf>
21. Société de Pneumologie de Langue Française, Société Française d'Anesthésie Réanimation, Société Française de Cardiologie, Société Française de Médecine du Travail, Société Française d'ORL, Société de Physiologie, et al. [Recommendations for clinical practice. Obstructive sleep apnea hypopnea syndrome in adults]. *Rev Mal Respir*. 2010;27(7):806-33.
22. Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T, et al. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. *Diabetes Care*. 2019;42(8):1593-603.
23. International Hypoglycaemia Study Group. Glucose Concentrations of Less Than 3.0 mmol/L (54 mg/dL) Should Be Reported in Clinical Trials: A Joint Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2017;40(1):155-7.
24. Manin G, Pons A, Baltzinger P, Moreau F, Iamandi C, Wilhelm JM, et al. Obstructive sleep apnoea in people with Type 1 diabetes: prevalence and association with micro- and macrovascular complications. *Diabet Med J Br Diabet Assoc*. 2015;32(1):90-6.

**Correspondence to:**

Jean-Daniel Lalau ([Lalau.Jean-Daniel@chu-amiens.fr](mailto:Lalau.Jean-Daniel@chu-amiens.fr))

Service d'Endocrinologie, Diabétologie et Nutrition, hôpital Nord, CHU Amiens-Picardie, Amiens 80054 Cedex 01, France.

Tel: +33 3 22 45 57 96

Fax: +33 3 22 45 53 34

## Legend to the figure

**Figure 1:** Prevalence of sleep-disordered breathing (SDB) in people with Type 1 diabetes and comparison to the prevalence expected in general population according to Peppard (18) (see Methods). SDB was defined as an apnoea-hypopnoea index (AHI)  $\geq 5/h$ . Severity of SDB was defined as mild with an AHI  $\geq 5/h$  and  $< 15/h$ , moderate with an AHI  $\geq 15/h$ -and  $< 30/h$  and severe with an AHI  $\geq 30/h$ .

**Table 1:** Characteristics of the study population as a function of the severity of SDB (either mild or absent, AHI <15/h, or moderate-to-severe, AHI ≥15/h).

	Total (n=46)	Absence of SDB or mild SDB only (n=38)	Moderate-to-severe SDB (n=8)	p-value
<i>Demography</i>				
Sex				
Male	25 (54.3)	17 (44.7)	8 (100.0)	0.005
Female	21 (45.7)	21 (55.3)	0 (0)	
Age, years	42 [35-54]	41 [32-50]	50 [41-61]	0.068
Diabetes duration (years)	18 [13-29]	16 [11-28]	26 [18-31]	0.117
Insulin therapy				
Insulin pump	30 (65.2)	25 (65.8)	5 (62.5)	1.0
Multiple daily injections	16 (34.8)	13 (34.2)	3 (37.5)	
HbA1c (mmol/mol)	60 [53-69]	57 [52-67]	70 [63-75]	0.053
HbA1c (%)	7.6 [7.0-8.5]	7.4 [6.9-8.3]	8.6 [7.9-9.0]	0.053
Weight (kg)	72.6 [65.8-83.5]	69.4 [64.5-80.5]	92.2 [80.5-97.2]	<0.001
BMI (kg/m <sup>2</sup> )	24.8 [23.0-28.9]	24.5 [22.2-26.9]	29.8 [27.8-31.1]	0.004
Normal weight: 18-24.9	24 (52.2)	23 (60.5)	1 (12.5)	
Overweight: 25-29.9	14 (30.4)	11 (28.9)	3 (37.5)	
Obese: ≥30	8 (17.4)	4 (10.5)	4 (50.0)	
Waist circumference (cm)	86.5 [77.0-98.0]	83.5 [76.0-92.0]	104.0 [100.0-114.5]	<0.001
Male	95.0 [83.5-104.0]	87.0 [81.0-97.5]	104.0 [100.0-114.5]	0.001
Female	77.0 [74.5-90.0]	77.0 [74.5-90.0]		
Neck circumference (cm)	37.0 [35.0-39.0]	36.5 [35.0-38.0]	41.5 [39.5-43.8]	<0.001
Hypertension	11 (23.9)	5 (13.2)	6 (75.0)	0.001
Lipids				
HDL (g/l)	0.56 [0.46-0.64]	0.56 [0.46-0.67]	0.55 [0.51-0.62]	0.664
LDL (g/l)	0.98 [0.83-1.19]	0.97 [0.84-1.11]	1.08 [0.78-1.49]	0.603
Triglycerides (g/l)	0.76 [0.66-1.04]	0.76 [0.66-0.99]	1.04 [0.64-1.27]	0.237
Cardiovascular risk				
Very high risk	27 (58.7)	20 (52.6)	7 (87.5)	
High risk	11 (23.9)	11 (28.9)	0 (0.0)	
Moderate risk	8 (17.4)	7 (18.4)	1 (12.5)	
Sedentary lifestyle	21 (46.7)	16 (43.2)	5 (62.5)	0.443
Tobacco use				
Never-smoker	25 (54.3)	20 (52.6)	5 (62.5)	
Active smoker	11 (23.9)	10 (26.3)	1 (12.5)	
Former smoker	10 (21.7)	8 (21.1)	2 (25.0)	
Cardiovascular outcomes				

Coronary artery disease	4 (8.9)	1 (2.7)	3 (37.5)	
Cerebrovascular stroke	3 (6.5)	0 (0)	3 (37.5)	
Peripheral vascular disease	3 (6.5)	1 (2.6)	2 (25.0)	
Retinopathy	15 (32.6)	9 (23.7)	6 (75.0)	
Nephropathy	4 (8.7)	1 (2.6)	3 (37.5)	
Neuropathy				
Peripheral neuropathy	8 (17.4)	5 (13.2)	3 (37.5)	
Autonomic neuropathy (n=30)	11/30 (36.7)	8/25 (32.0)	3/5 (60.0)	
<hr/> <i>Sleep characteristics</i>				
Epworth sleepiness scale score >10	11 (23.9)	10 (26.3)	1 (12.5)	
Number of symptoms suggestive of SDB	4 [2-5]	4 [2-5]	4 [2-5]	0.767
Sleep efficiency (%)	86.5 [80.4-92.9]	88.2 [82.8-93.5]	79.8 [72.9-88.3]	0.064
NREM stage 1 (%)	8.3 [4.2-13.4]	6.7 [3.6-12.3]	8.8 [6.5-14.2]	0.262
NREM stage 2 (%)	53.9 [49.2-59.0]	52.5 [49.0-57.2]	57.1 [54.6-60.7]	0.089
NREM stage 3 (%)	20.0 [15.4-25.0]	20.5 [15.4-25.4]	19.0 [15.0-20.3]	0.286
REM (%)	16.7 [13.6-21.2]	17.1 [14.6-21.4]	12.4 [8.7-20.8]	0.152
Micro-arousal index (/h)	8.1 [5.4-12.3]	7.2 [4.8-10.4]	12.2 [9.6-25.4]	0.003
WASO (%)	11.9 [8.4-16.6]	10.6 [7.8-15.8]	16.7 [13.6-27.9]	0.006
<hr/> <i>Glucose variability</i>				
Coefficient of variation >36%	22 (47.8)	17 (44.7)	5 (62.5)	0.451
Glucose level <70 mg/dl	19 (41.3)	14 (36.8)	5 (62.5)	0.246
Glucose level <54 mg/dl	13 (28.3)	9 (23.7)	4 (50.0)	0.143

Data are expressed as the n (%) or the median [IQR].

AHI: apnoea-hypopnoea index; BMI: body mass index; HDL: high-density lipoprotein; LDL: low-density lipoprotein; NREM: non-rapid eye movement (NREM sleep was divided into 3 stages according to The American Academy of Sleep Medicine (20)); REM: rapid eye movement; WASO: wakefulness after sleep onset; SDB: sleep-disordered breathing.

**Table 2:** Sleep characteristics according to within or above-target glucose variability (%CV-CGM  $\leq$ 36% or  $>$ 36%, respectively).

	Within (n = 24)	Above (n = 22)	p-value
<b>Sleep</b>			
Epworth sleepiness scale $>$ 10	6 (25.0)	5 (22.7)	1.0
Number of symptoms suggesting SDB	4 [2-6]	4 [2-5]	0.873
Sleep efficiency (%)	87.0 [80.0-92.6]	86.5 [81.5 – 93.3]	0.900
NREM1 (%)	8.7 [3.9-13.2]	5.6 [4.2 – 13.7]	0.657
NREM2 (%)	54.2 [50.7-57.2]	53.2 [48.3 – 60.7]	0.773
NREM3 (%)	19.1 [15.3-24.4]	20.5 [17.5 – 25.4]	0.590
REM (%)	16.7 [14.2-19.5]	17.1 [11.8 – 23.3]	0.883
Micro-arousal index (/h)	8.8 [6.1-13.6]	7.6 [4.8 – 10.5]	0.353
WASO (%)	13.0 [9.8-17.0]	10.2 [7.8 – 16.5]	0.287
AHI (/h)	4.4 [1.3-12.2]	2.7 [0.8 – 12.7]	0.516
AHI $>$ 15/h	3 (12.5)	5 (22.7)	0.451

Data are expressed as the n (%) or the median [IQR].

%CV-CGM: coefficient of variation of glucose values using continuous glucose monitoring; AHI: apnoea-hypopnoea index; BMI: body mass index; NREM: non-rapid eye movement (NREM sleep was divided into 3 stages according to The American Academy of Sleep Medicine (20)); REM: rapid eye movement; WASO: wakefulness after sleep onset.



**Table 3:** Sleep characteristics according to the presence or not of glucose levels below 70 or 54 mg/dl.

	Below 70 mg/dl			Below 54 mg/dl		
	Absence (n = 27)	Presence (n = 19)	p-value	Absence (n = 27)	Presence (n = 19)	p-value
Sleep						
Epworth sleepiness scale >10	4 (14.8)	7 (36.8)	0.159	7 (21.2)	4 (30.8)	0.702
Number of symptoms suggesting SDB	4 [2-5]	4 [2-5]	0.880	2 [4-5]	3 [4-7]	0.655
Sleep efficiency (%)	85.8 [80.0-92.2]	86.7 [80.5-93.4]	0.753	88.2 [80.0 – 93.1]	86.2 [81.2 – 92.7]	0.919
NREM stage 1 (%)	9.1 [4.4-13.8]	5.2 [4.1-10.4]	0.296	8.6 [4.0 – 13.6]	5.9 [4.2 – 9.7]	0.524
NREM stage 2 (%)	52.3 [48.9-56.7]	54.8 [50.4-62.5]	0.208	54.1 [49.1 – 56.9]	53.6 [49.8 – 62.5]	0.422
NREM stage 3 (%)	19.8 [15.5-25.5]	20.1 [11.3-24.4]	0.212	19.8 [15.5 – 25.4]	20.1 [12.6 – 23.3]	0.443
REM (%)	16.4 [14.2-19.0]	19.4 [11.1-25.1]	0.349	16.4 [14.3 – 19.4]	19.4 [10.4 – 25.4]	0.337
Micro-arousal index (/h)	8.0 [5.2-12.8]	8.9 [5.4-10.6]	0.912	8.6 [5.6 – 12.8]	6.8 [4.8 – 10.2]	0.499
WASO (%)	13.7 [9.6-17.2]	10.2 [8.3-16.2]	0.476	13.7 [9.7 – 17.4]	9.9 [7.9 – 15.1]	0.268
AHI (/h)	3.8 [1.0-11.7]	2.7 [0.5-15.2]	0.978	3.8 [1.1 – 11.9]	2.7 [0.5 – 15.3]	1.0
AHI >15/h	3 (11.1)	5 (26.3)	0.246	4 (12.1)	4 (30.8)	

Data are expressed as the n (%) or the median [IQR].

AHI: apnoea–hypopnoea index; BMI: body mass index; NREM: non-rapid eye movement (NREM sleep was divided into 3 stages according to The American Academy of Sleep Medicine (20)); REM: rapid eye movement; WASO: wakefulness after sleep onset.

Table 4: Spearman coefficients for the correlations between AHI on one hand and BMI, waist circumference, neck circumference, and glucose variability on the other.

	Total (n=46)	Male (n=25)	Female (n=21)
IAH / BMI	0.47 (p = 0.001)	0.68 (p < 0.001)	0.25 (p = 0.281)
IAH / waist circumference	0.67 (p < 0.001)	0.75 (p < 0.001)	0.40 (p = 0.072)
IAH / neck circumference	0.60 (p < 0.001)	0.72 (p < 0.001)	0.22 (p = 0.339)
IAH / %CV-CGM	-0.04 (p = 0.770)	0.07 (p = 0.758)	-0.06 (p = 0.786)

AHI: apnoea–hypopnoea index; BMI: body mass index; %CV-CGM: coefficient of variation in the blood glucose level, according to continuous glucose monitoring.

**Figure 1**

