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Subjective sleep disturbances and glycemic control in adults with long-standing type 1 diabetes: The Pittsburgh's Epidemiology of Diabetes Complications study

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ABSTRACT

Aims: To date, studies on sleep disturbances in type 1 diabetes (T1D) have been limited to youth and/or small samples. We therefore assessed the prevalence of subjective sleep disturbances and their associations with glycemia and estimated insulin sensitivity in individuals with long-standing T1D.

Methods: We conducted a cross-sectional study including 222 participants of the Epidemiology of Diabetes Complications study of childhood-onset T1D attending the 25-year examination (mean age = 52 years, diabetes duration = 43 years). The Berlin Questionnaire (risk of obstructive sleep apnea, OSA), the Epworth Sleepiness Scale (daytime sleepiness), and the Pittsburgh Sleep Quality Index (sleep quality, bad dreams presence, and sleep duration) were completed. Associations between sleep disturbances and poor glycemic control ($HbA_{1c} \geqslant 7.5\%/58$ mmol/mol), log-transformed HbA_{1c}, and estimated insulin sensitivity (estimated glucose disposal rate, eGDR, squared) were assessed in multivariable regression.

Results: The prevalences of high OSA risk, excessive daytime sleepiness, poor sleep quality, and bad dreams were 23%, 13%, 41%, and 26%, respectively, with more women (51%) reporting poor sleep quality than men (30%, $p = 0.004$). Participants under poor glycemic control were twice as likely to report bad dreams ($p = 0.03$), but not independently ($p = 0.07$) of depressive symptomatology. Sleep duration was directly associated with HbA_{1c} among individuals with poor glycemic control, but inversely in their counterparts (interaction $p = 0.002$), and inversely associated with eGDR ($p = 0.002$).

Conclusions: These findings suggest important interrelationships between sleep, gender, depressive symptomatology, and glycemic control, which may have important clinical implications. Further research is warranted to examine the mechanism of the interaction between sleep duration and glycemic control.

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1. Introduction

Two related chronic conditions, diabetes and sleep disorders, have increased over the past few decades [1–3]. Disturbed sleep is associated with burdensome public health conditions including incident hypertension [4], coronary heart disease [5,6], stroke [5,7], and even all-cause mortality [5]. Importantly, the association between sleep disturbance and diabetes appears to be bidirectional, e.g. poor sleep quality can worsen diabetes control, while diabetes complications can impair sleep quality [8]. The majority of studies linking sleep disturbances and diabetes have focused on type 2 diabetes [9–11] and obesity risk factors. Sleep disturbances in type 1 diabetes (T1D) have been studied, however, most research has been limited to youth [12–14] and/or samples of less than 50 individuals [12–15]. As obesity has been increasing among persons with T1D [16], studying the role of disturbed sleep in this population has now become even more relevant.

The prevalence of sleep-disordered breathing in T1D [17–20] appears somewhat similar to that in the general population, however, without a male preponderance [21]. For instance, polysomnography-measured moderate-to-severe obstructive sleep apnea (OSA, apnea hypopnea index (AHI) >10 events/hour) in a T1D study by Manin et al. was present among 46%, while the prevalence of severe OSA (AHI $\geqslant$ 30 events/hour) was 19% [20]. No gender difference was present in this study [20]. In another T1D cohort, Schober and colleagues observed a lower moderate-to-severe OSA prevalence (10.3%), although defined as AHI $\geqslant$ 15 events/hour, but did not find differences by gender [19]. In a small T1D pilot study ($n = 40$), Borel et al. observed a high prevalence of OSA (40%) defined as AHI > 15 events/per hour or OSA treatment, but did not assess gender differences [18]. In contrast to the T1D studies by Manin et al. [20] and Schober et al. [19], a profound gender difference in moderate-to-severe sleep-disordered breathing defined by the current 2012 American Academy of Sleep Medicine criterion [22] (AHI $\geqslant$ 15 events/hour) has been recently reported in the general population (i.e. 23.4% in women; 49.7% in men) [21].

The variability in the prevalence of OSA/sleep-disordered breathing in T1D mainly stems from differences in methodologies and definitions used to characterize disturbed sleep [18–20]. Although polysomnography is the gold standard for diagnosing sleep disorders, it is rarely feasible to implement in large epidemiological studies. Additionally, screening tools for different sleep disturbances are widely available and easy to implement. However, to the best of our knowledge, only one previous study measured various sleep disturbances in T1D adults using several validated sleep questionnaires, but did not assess gender differences [17].

The relationship between disturbed sleep and glycemic control among adults with T1D is inconsistent. While some studies observed non-significant associations [17,18,20] between sleep disturbances (e.g. poor sleep quality, excessive daytime sleepiness, high-risk OSA) and hemoglobin A_{1c} (HbA_{1c}), positive associations have also been reported (i.e. with excessive daytime sleepiness, shorter sleep duration, and shorter deep sleep time) [19,23,24]. The effect of disturbed sleep on insulin resistance/sensitivity in T1D is also unclear. Nevertheless, a previous T1D study demonstrated a decrease in peripheral insulin sensitivity in seven participants after only one night of restricting sleep duration to four hours [15].

The objectives of our study were therefore to determine the overall and gender-specific prevalence of subjective sleep disturbances using three validated sleep questionnaires and to assess cross-sectional relationships between sleep disturbances and both glycemic control and estimated insulin sensitivity in a well-characterized cohort of adults with long-standing, childhood-onset T1D.

2. Materials and methods

The study population comprised participants from the Pittsburgh Epidemiology of Diabetes Complications (EDC) study – an ongoing, 25-year prospective cohort of childhood-onset (<17 years) T1D [25,26]. The EDC was based on individuals diagnosed with incident T1D, or seen within one year of diagnosis, at Children's Hospital of Pittsburgh between 1950 and 1980. In order to participate in EDC, participants had to reside within a two hours' drive or 100 miles from the EDC clinic. This cohort was previously shown to be representative of the T1D population in Allegheny County, Pennsylvania [27]. At baseline (1986–1988), participants ($n = 658$) were on average 28 years old and had a mean diabetes duration of 19 years. They were re-examined or surveyed every two years post baseline. The study protocol was approved by the University of Pittsburgh Institutional Review Board and a written informed consent was provided prior to any study procedure.

During the most recent, 25-year clinical examination (2011–2014), three validated sleep questionnaires, the Pittsburgh Sleep Quality Index [28] (PSQI), the Epworth Sleepiness Scale [29] (ESS), and the Berlin Questionnaire [30] (BQ), were used for the first time to assess sleep quality, excessive daytime sleepiness, and OSA risk, respectively. The PSQI was self-administered prior to the clinical examination. During the clinical exam, the BQ and ESS were administered by a trained research specialist who also inquired about a history of diagnosed OSA. Out of 376 in-area, exam-eligible participants, 222 (59%) completed the BQ and the ESS, while 196 (52%) fully completed the PSQI. One participant attended the exam but did not complete the sleep questionnaires.

2.1. *Subjective sleep disturbances*

The PSQI assesses sleep quality and disturbance during the past month [28]. It consists of 19 self-rated questions and five questions rated by a roommate or bed partner which are not calculated into the total score. The 19 questions are grouped into seven component scores (i.e. sleep quality, latency, duration, efficiency, disturbances, sleep medication use, and daytime dysfunctions), weighted equally from 0 to 3. Higher scores indicate worse sleep quality. A global PSQI score is a sum of all component scores (range, 0–21). We used the standard cut-off point to define poor sleep quality (PSQI global score > 5). As a proxy for disturbed rapid eye movement (REM) sleep, which has been linked to poor glycemic control