Impact of SHE Frequency and IAH Status on Sleep Quality in Adult Continuous Glucose Monitor Users With Type 1 Diabetes: Results from a Cross-Sectional Survey Study

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INTRODUCTION

- Type 1 diabetes (T1D) is a lifelong chronic metabolic condition characterized by endogenous insulin deficiency leading to abnormal glucose regulation.[1] People with T1D (pwT1D) require lifelong exogenous insulin therapy and should aim to keep their hemoglobin A1c (HbA1c) levels <7%, according to the American Diabetes Association guidelines[2-3]
- Despite using advanced diabetes technologies such as continuous glucose monitors (CGM) and automated insulin delivery systems, many pwT1D are not meeting these guideline targets and experience severe hypoglycemic events (SHEs)[3-4]
- SHEs are characterized by altered mental and/or physical status, requiring the assistance of a third party for recovery. Repeated episodes of hypoglycemia can result in impaired awareness of hypoglycemia (IAH), further increasing the risk of SHEs. SHEs are associated with acute and chronic complications such as seizures, comas, and even death[4]
- While many pwT1D report overnight fear of SHEs, data describing the impact of SHEs and IAH on sleep quality in many pwT1D is limited

OBJECTIVE

To describe the impact of SHEs and IAH on sleep quality in adult CGM users with T1D

METHODS

Study Design

- An online cross-sectional survey was administered to people with T1D from the T1D Exchange Registry

Key Inclusion Criteria

- Self-reported clinical diagnosis of T1D ≥5 years
- Current CGM user
- Aged ≥18 years old

Survey Design & Administration

- SHE frequency was collected through participant responses to the question:
  - "A severe hypoglycemic event (SHE) is a low blood sugar where you experience a change in your mental or physical status (like increased confusion or loss of consciousness) and where you need help from another person to recover. How many times did you experience a severe hypoglycemic event in the past 12 months?"
- IAH status was determined using established cutoffs from the modified Gold score.[5] The Gold score is a 1-item questionnaire that asks individuals to report their experience in detecting hypoglycemic events with responses ranging from 1 (always aware) to 7 (never aware) in a Likert type scale
  - A score of ≤2 = normal awareness (IAH–); 3 = borderline (undetermined); ≥4 suggests impaired awareness of hypoglycemia (IAH+)
- Self-reported sleep disorder was measured with a bespoke question "Have you ever been diagnosed with or treated by a medical professional for any of the following conditions…"
  - Sleep disorder was listed as one of the conditions
  - Response options included Yes, No, and Unsure
- Sleep quality was assessed using a modified version of the single-item sleep quality scale (mSQS)[6]
  - The following question refers to your overall sleep quality for the majority of nights in the **past 7 days ONLY.**
  - Please think about the quality of your sleep overall such as how many hours of sleep you got, how easily you fell asleep, how often you woke up in the middle of the night (except to go to the bathroom), how often you woke up earlier than you had to in the morning, and how refreshing your sleep was.
  - **During the past 7 days, how would you rate your sleep quality overall?**
    - *Rate your sleep quality on a scale of 0 ("Terrible") to 10 ("Excellent"). A higher score means better sleep quality*

Cohort Definitions

- Cohorts were defined[7] based on self-reported SHE frequency the past 12 months and IAH status (modified Gold score)

Table 1. Study Design

Cohort	Definition
Problematic SHEs	Individuals with SHE 1+/IAH+ or SHE 2+/IAH-
Single SHE, no-IAH	Individuals with 1 SHE and IAH-
Undetermined IAH	Individuals with SHE ≥0 and modified Gold score = 3
No-SHE	Individuals with 0 SHE and IAH+ or 0 SHE and IAH-

IAH: impaired awareness of hypoglycemia; **SHE:** severe hypoglycemic event

Statistical Analysis

- Descriptive analyses (mean, standard deviation [SD], counts, percentages) of participant demographics and clinical characteristics are reported for the Problematic SHEs and No-SHE cohorts
- Participant responses to the mSQS were summarized descriptively, reported for Problematic SHEs and No-SHE cohorts and further stratified by insulin delivery method: Hybrid closed-loop system/ do-it-yourself (HCLS/DIY), Predictive low glucose suspend (PLGS), Pump without automated insulin-delivery (pump no-AID), and multiple daily injections (MDI)

RESULTS

- Results are summarized by the Problematic SHEs (N=375) and No-SHE (N=1033) cohorts (**Table 2**). Relative to the No-SHEs cohort, participants in the Problematic SHEs cohort were slightly older (mean age = 49.0 [SD = 14.6] vs. 45.6 [SD=15.7] years) (**Table 2**)
- More participants in the No-SHE cohort used HCLS/DIY (69.0%) relative to the Problematic SHEs cohort (55.7%). Endocrinologist use between the Problematic SHEs and No-SHE cohorts were similar (77.3% vs. 77.7%) (**Table 2**)
- Participants with Problematic SHEs self-reported numerically higher rates of sleep disorder relative to the No-SHE cohort (28.8% vs. 16.6%) (**Table 2**)

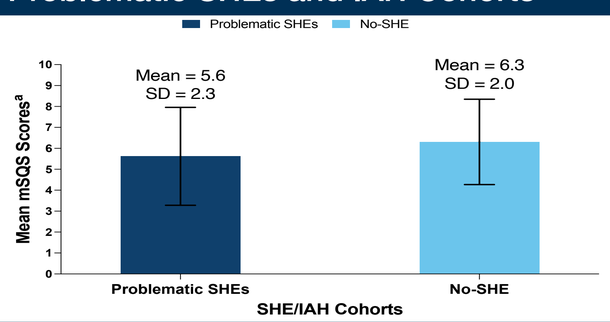
Table 2. Participant Demographics & Clinical Characteristics[a]

	Problematic SHEs[b] (N=375, 20.3%)	No-SHE[b] (N=1033, 55.9%)
Age (years), mean (SD)	49.0 (14.6)	45.6 (15.7)
Gender, n (%)		
Male	108 (28.8)	354 (34.3)
Female	266 (70.9)	666 (64.5)
Non-binary / genderqueer	1 (0.3)	11 (1.1)
Prefer to self-identify	0 (0)	1 (0.1)
Prefer not to answer	0 (0)	1 (0.1)
Race, n (%)		
American Indian/Alaskan Native	3 (0.8)	5 (0.5)
Asian	1 (0.3)	10 (1.0)
Black/African American	21 (5.6)	13 (1.3)
Native Hawaiian or Other Pacific Islander	1 (0.3)	1 (0.1)
North African/Middle Eastern	1 (0.3)	7 (0.7)
White/Caucasian	324 (86.4)	958 (92.7)
Mixed Race	18 (4.8)	32 (3.1)
Other	6 (1.6)	7 (0.7)
Ethnicity – Hispanic or Latino, n (%)	23 (6.1)	55 (5.3)
Most recent HbA1c, mean (SD)	6.9 (1.1)	6.6 (0.9)
Medical emergency treatment for T1D (excluding SHEs) in the past 12 months, n (%)	52 (13.9)	60 (5.8)
Diabetes technology subtypes, n (%)		
HCLS/DIY	209 (55.7)	713 (69.0)
PLGS	33 (8.8)	55 (5.3)
Pump no-AID	52 (13.9)	119 (11.5)
MDI	81 (21.6)	146 (14.1)
Selected Complications, n (%)		
Microvascular		
Nephropathy	31 (8.3)	47 (4.5)
Neuropathy	92 (24.5)	108 (10.5)
Retinopathy	106 (28.3)	222 (21.5)
Macrovascular		
Cerebrovascular disease	8 (2.1)	24 (2.3)
Cardiovascular disease	47 (12.5)	57 (5.5)
Vascular disease	29 (7.7)	40 (3.9)
Hypothyroidism	90 (24.0)	275 (26.6)
Hypertension	152 (40.5)	317 (30.7)
Dyslipidemia	155 (41.3)	371 (35.9)
Joint or bone issues	191 (50.9)	366 (35.4)
Autoimmune disease	90 (24.0)	246 (23.8)
Sleep disorder	108 (28.8)	171 (16.6)
Depression	184 (49.1)	325 (31.5)
Anxiety	175 (46.7)	341 (33.0)

[a]Table 2 was previously presented elsewhere.
[b]The Overall sample also included Single SHE, no-IAH (n=102) and Undetermined IAH (n=337) cohorts.
AID: automated insulin delivery; **HbA1c:** hemoglobin A1c; **HCLS/DIY:** hybrid closed loop system/ do-it-yourself; **IAH:** impaired awareness of hypoglycemia; **PLGS:** pump no automated insulin delivery; **MDI:** multiple daily injection; **SD:** standard deviation; **T1D:** type 1 diabetes

- Participants in the Problematic SHEs cohort reported numerically lower mean sleep quality (lower mSQS score) compared to the No-SHEs cohort (5.6 [SD=2.3] vs. 6.3 [SD=2.0]) (**Figure 1**)

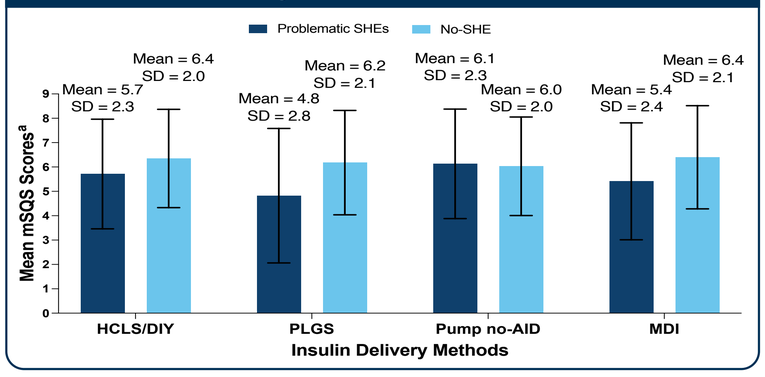
Figure 1. Mean mSQS Scores Between Problematic SHEs and IAH Cohorts



IAH: impaired awareness of hypoglycemia; **SHE:** severe hypoglycemic event; **mSQS:** modified Sleep Quality Scale
[a]Error bars = SD

- Participants with Problematic SHEs reported numerically lower mean sleep quality (lower mean mSQS score) compared to participants in the No-SHEs cohort, except from Pump no-AID users, where mSQS scores were similar between cohorts (**Figure 2**)
- Between Problematic SHEs and No-SHE cohorts, largest numerical difference in mean mSQS scores was observed in PLGS (4.8 [SD=2.8] vs. 6.2 [SD=2.1]), followed by MDI (5.4 [SD=2.4] vs. 6.4 [SD=2.1]), HCLS/DIY (5.7 [SD=2.3] vs. 6.4 [SD=2.0]) and Pump no-AID (6.1 [SD=2.3] vs. 6.0 [SD=2.0]) (**Figure 2**)

Figure 2. Numerical Comparison of Mean mSQS Scores Between the Problematic SHEs and No-SHE Cohorts and Stratified by Insulin Delivery Methods



Note: Stratification of SHE/IAH cohorts by insulin delivery methods resulted in unequal group sizes: HCLS/DIY (Problematic SHEs [n=205] vs. No-SHE [n=712]); PLGS (Problematic SHEs [n=33 vs. No-SHE [n=55]); Pump no-AID (Problematic SHEs [n=52] vs. No-SHE [n=119]); MDI (Problematic SHEs [n=81] vs. No-SHE [n=146])
[a]Error bars = SD
AID: automated insulin delivery; **HCLS/DIY:** hybrid close loop system/do-it-yourself; **IAH:** impaired awareness of hypoglycemia; **MDI:** multiple daily injection; **PLGS:** predictive low glucose suspend systems; **SHE:** severe hypoglycemic event; **mSQS:** modified Sleep Quality Score

Limitations

- Study participants were from the T1D Exchange Registry, a cohort of individuals with T1D who tend to be highly engaged, have a high degree of diabetes technology use, and have historically been shown to be more likely to achieve glycemic targets
- Study participants were mostly White, non-Hispanic or Latino, identified as female, highly educated, were self-selected and needed access to the internet and email, which may all impact the generalizability of these results
- All data were self-reported; eligibility and clinical data were not verified by a clinician
- Analysis conducted were descriptive; associations between sleep quality and SHE frequency/IAH status were not assessed

CONCLUSIONS

- **Compared to the No-SHE cohort, participants with Problematic SHEs self-reported numerically higher medical emergency treatments (excluding SHEs), potentially suggesting higher frequency or more severe comorbidities**
- **Participants with Problematic SHEs reported numerically lower sleep quality compared to those without SHE (No-SHE cohort)**
  - **Numerically higher self-reported rates of sleep disorder (28.8% vs. 16.6%)**
  - **Lower sleep quality (lower total mean mSQS scores) across insulin delivery methods, except for pump-no-AID users, where total mean mSQS scores between the cohorts were similar**
- **Collectively, these findings suggest a potential link between SHE frequency and impaired sleep quality, which may affect QoL of pwT1D. Future research should evaluate the association between SHE frequency, IAH status and sleep quality across different insulin delivery methods**
- **These findings also show how different insulin delivery methods may influence sleep quality in pwT1D and SHEs and highlight the need for innovative therapies beyond insulin delivery methods.**

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Author Disclosures

CSK, **HN**, **KSC**, **EMC**, and **WAW** are employees of T1D Exchange. **WHP** has served as a consultant for Dexcom, Abbott Diabetes, Eli Lilly, Sanofi, Novo Nordisk, Vertex Pharmaceuticals, Embecta, Mannkind, Ascensia, and Sequel. **WHP** received research support from Dexcom and Abbott Diabetes. **ABK**, **PC**, **KC**, **DB**, and **LC** are employees of Vertex Pharmaceuticals and may hold stock or stock options in the company

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