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Glycemic control and its association with sleep quality and duration among type 2 diabetic patients

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ABSTRACT

Background: Poor glycemic control is the current most important tragedy in type 2 diabetic patients. Sleep has a major modulatory effect on endocrine and metabolic function. Sleep disturbance is associated with increased circulating cortisol levels, sympathetic activity, and epinephrine secretion. These physiological conditions are directly or indirectly associated with glucose metabolism in our body cells. In Ethiopia, sleep pattern association with glycemic control level is not studied yet.

Objectives: To assess glycemic control and its association with sleep quality, sleep duration and napping among patients with type 2 diabetes mellitus in Felege Hiwot Comprehensive Referral and Specialized Hospital Northwest Ethiopia.

Method: An institutional-based cross-sectional study was conducted among 407 type 2 diabetes mellitus patients from July 1, 2020, to April 28, 2021, using a systematic random sampling technique. We drew 5 mL of blood from each patient before breakfast to determine their fasting blood sugar level. The Pittsburg Sleep Quality Index was used to assess patients' sleep quality, and the presence or absence of Obstructive Sleep Apnea was determined using the STOP-BANG questionnaire. Data were analysed using STATA version 14.1.variables with a P-value of <0.05 were considered statistically significant.

Results: Glycemic control was found to be poor in 54.05% of the study participants. Female sex, poor sleep quality, and short and long sleep durations were all significantly associated with impaired glycemic control. Being female increased the odds of poor glycemic control by 2.7 times (AOR = 2.7, 95% CI: 1.23, 6.15) compared to males. T2DM patients who had poor sleep quality had 3.3 times (AOR = 3.3, 95% CI (1.16, 9.37) higher odds of poor glycemic control compared to patients who had good sleep quality. The odds of having poor glycemic control among T2DM patients who were at low risk of OSA and intermediate risk of OSA were decreased by 96% (AOR = 0.03, 95% CI: 0.01, 0.12) and 86% (AOR = 0.14, 95% CI: 0.05, 0.43) compared to T2DM patients who were at high risk of OSA, respectively. T2DM patients who had short sleep duration (<6 hours) were 8.3 times (AOR = 8.3, 95% CI: 2.66–25.85) higher chances of poor glycemic control compared to patients who had average sleep duration. T2DM patients who had long sleep duration (>8 hours) increased the odds of poor glycemic control by 2.6 times (AOR = 2.6, 95% CI (1.12–6.04) compared to those who had average sleep duration. The chances of having poor glycemic control among T2DM patients who did not take the balanced diet recommended by their physician were increased by 3.8 times (AOR = 3.8 95% CI: 1.05–13.77).

Conclusion: The prevalence of poor glycemic control in T2DM patients was high. Poor sleep quality, both short and long sleep duration, and an intermediate or low risk of obstructive sleep apnea were statistically associated with poor glycemic control. Hence, good sleep quality and appropriate sleep duration are recommended to maintain glycemic control levels in the normal range.

1. Introduction

Diabetes mellitus (DM) is a group of metabolic disorders that share hyperglycemia as a common characteristic [1]. Type 1 Diabetes Mellitus (T1DM) is characterized by absolute insulin deficiency due to autoimmune -cell destruction [2], whereas Type 2 Diabetes Mellitus (T2DM) is

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Table 1
Sociodemographic characteristics of T2DM patients attending at in Felege Hiwot Comprehensive Referral and Specialized Hospital,Northwest Ethiopia, 2021.

Variable		frequency	Percent
Age (years)	Age ≤24	3	0.74
	25–44	140	34.4
	45–64	195	47.9
	Age ≥65	69	16.95
Sex	Male	220	54.05
	Female	187	45.95
Residence	Urban	251	61.67
	Rural	156	38.33
Occupation	Farmers	70	17
	Merchant	39	9.58
	Government employ	117	28.75
	Self-employed	54	13.27
	Housewife	84	20.64
	Jobless	43	10.57
Marital status	Married	278	68.3
	Single	48	11.79
	Widowed	41	10.07
	Divorced	40	9.83
Educational status	Illiteratenot read and write	139	34.15
	Primary	85	20.88
	Secondary	75	18.43
	College & above	108	26.54

Table 2
The clinical, anthropometric, and behavioral characteristics of T2DM patients attending at Felege Hiwot Comprehensive Referral and Specialized Hospital Northwest Ethiopia, 2021.

Variable		Frequency	Percent
DM[a] duration	<7 year	225	55.28
	≥7year	182	44.72
Family history of DM	Yes	108	26.54
	No	299	73.46
Drug regimen	Insulin	159	39.07
	Metformin	177	43.49
	Mixed	71	17.44
Body mass index	Underweight	14	3.44
	Normal	236	57.99
	Overweight	128	31.45
	Obese	29	7.13
Hypertension	Yes	151	37.1
	No	256	62.9
DM complication	No	266	65.33
	Retinopathy	70	17.2
	Nephropathy	30	7.4
	Others**	41	10.07
Drug adherence	Low	52	12.78
	Medium	46	11.3
	High	309	75.92
Sleep quality	Good	269	66.09
	Poor	138	33.91
Napping	Yes	127	31.2
	No	280	68.8
Dinner time	Before 8: pm.	115	28.26
	After 8: pm.	292	71.74
Exercise	Yes	287	70.52
	No	120	29.48
Diet	Yes	350	86
	No	57	14

[a] DM: Others**:Neuropathy + Cardiac + Others.

characterized by insulin resistance, impaired insulin secretion, tissue insensitivity to insulin, and excessive hepatic glucose production [3].

Poor glycemic control is defined as an average fasting blood glucose (FBG) level 152 mg/dl in three measurements, which is comparable with HbA1C 7%, according to the American Diabetes Association (ADA) standards of medical care in diabetes [2]. Despite patients being on treatment, glycemic control is not achieved at the desired level. This is linked to the development of macro- and microvascular complications, either directly or indirectly. This is common in type-2 diabetes mellitus (T2DM), including extremity amputations, peripheral neuropathy, end-stage renal disease (nephropathy), cardiovascular disease, cerebrovascular disease, and retinopathy [4].

The prevalence of poor glycemic control in T2DM patients is increasing and variably reported worldwide. This was indicted in a study conducted in Malaysia (72%) [5]. Other research has found that poor glycemic control affects people in the United States 76% [6], Venezuela (76%) [7], Jordan (65.1%) [8], Hawaii (68.5%) [9], and Kenya (60.5%) [10].

Optimizing sleep duration and quality as a way of imp**roving glycemic control in T2DM** patients [11] Since sleep is linked to several hormonal changes that alter glucose metabolism, it is crucial to assess the association between sleep duration and sleep quality with glycemic control [4]. Glycemic control is the most challenging problem facing the Ethiopian T2DM population. However, no research had been conducted on sleep duration and sleep quality among DM patients. As a result, the focus of this research was to determine the magnitude of poor glycemic control and its association with sleep quality, sleep duration, and napping in Northwest Ethiopian T2DM patients.

2. Methods and materials

2.1. Study design, setting and participants

An institutional-based cross-sectional study was conducted on known T2DM patients who had treatment follow-up at Felege Hiwot Comprehensive Referral and Specialized Hospital's Chronic Disease Clinic from July 1, 2020, to April 28, 2021 (the study took 10 months due to the COVID protocol). The hospital is located in Bahir Dar, which is 560 km northwest of Ethiopia's capital city, Addis Ababa.

The hospital is the leading referral hospital in Northwest Ethiopia, next to the University of Gondar Comprehensive and Specialized Hospital, serving the middle population of the region. It employs 1041 people, including 121 physicians, 370 nurses, 59 midwives, 51 pharmacists, 72 laboratory technicians, and the remainder are administrative personnel.The hospital provides a referral service with >350 beds and serves >10 million people in the region. The DM follow-up service is one of the services given by this hospital, and there are more than 6000 registered DM patients.

All type 2 DM patients who visited a chronic illness follow-up clinic during the study period and were older than 18 years were included. While pregnant women, patients with a known psychiatric illness, severely ill patients, and patients who had not had consecutive month follow-up and recorded FBS were included in this study, pregnant women, patients with a known psychiatric illness, severely ill patients, and patients who had not had consecutive month follow-up and recorded FBS were excluded.

2.2. Sample size and sampling techniques

The sample size was calculated using a single population proportion formula, a 95% confidence level, a 5% margin of error, and a 10% nonresponse rate, as reported in a study conducted at the University of Gondar Comprehensive Referral and Specialized Hospital Gondar, Ethiopia [12]. The total number of participants was 407. In Felege Hiwot Comprehensive Referral and Specialized Hospital, there is one dedicated day per week for T2DM patients to have a follow-up in the chronic illness follow-up clinic. On average, 100 people come into the clinic for follow-up care in one day. a systematic random sampling technique to select study participants.

2.3. Data collection method

Face-to-face interviews with structured questions were used to collect data. It is used to collect information on sociodemographic data,

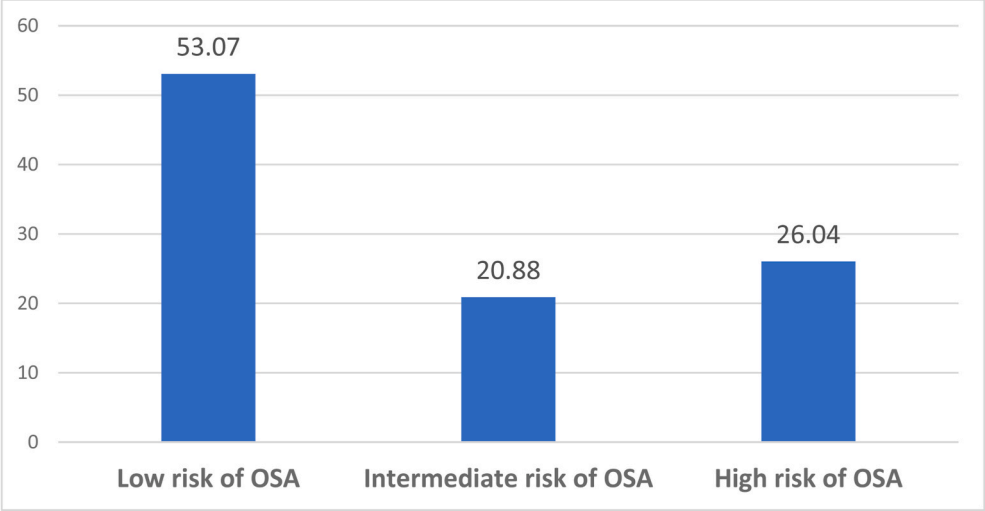

Fig. 1. The level of OSA in T2DM patients attending at Felege Hiwot Comprehensive Referral and Specialized Hospital Northwest Ethiopia, 2021.

such as sex, age, marital status, educational status, occupation, residence, and clinical and anthropometric data, including obstructive sleep apnea (OSA), DM duration in years, family history of DM, drug regimen, DM complications, hypertension, body mass index, waist circumference, and drug adherence, as well as lifestyle and habit data, including physical activity, sleep duration, sleep quality, and napping.

Data on the patients' fasting blood glucose (FBG) levels were taken either from their medical records if they had been tested within 3 months before the research encounter or they were tested during the study period. Each patient's glycemic level was coded as either poor or good. Poor glycemic control was defined in this study as an FBG level above 152 mg/dL [13].

About 5 ml *of blood was collected in the morning before breakfast, and the FBG level was determined by the glucose oxidase method using the MINDRAY BS-200E (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). The three measurements of FBG were used to estimate the average FBG level. Then, each patient's glycemic level was coded as either poor or good.*

The Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality of patients. The presence or absence of obstructive sleep apnea (OSA) in patients was checked by using the Brazilian version of the STOP-BANG questionnaire [14].

2.4. Data processing and analysis

Data were cleaned, coded, and entered into Epi Data version 3.1 Software and exported to STATA version 14.1 for further analysis. Poor glycemic control was defined in this study as FBG ≥152 mg/dl, which is comparable with >7% HbA1C according to ADA Standards of Medical Care in Diabetes [15]. According to Pittsburg sleep quality index a global score of more than five [5]indicates poorer sleep or poor sleep quality. Low risk of OSA is defined as 'yes 'to 0–2 questions, intermediate risk of OSA yes to 3–4 questions, and high risk of OSA yes to 5–8 questions [14]. Descriptive statistics, including tables, graphs, and charts were used. Model fitness was checked by using the Hosmer–Lemeshow test. Bivariabale and mutivaraible logistic regression anlysis were used to identify factors associated with poor glycemic control. Those variables with a p-value of ≤0.2 in the bivariable analysis were considered for multivariable logistic regression analysis. Variables with a P-value of <0.05 were considered statistically significant.

2.5. Ethical considerations

Ethical clearance was obtained from the Institutional Review Board of the School of Medicine, University of Gondar, with protocol number 1958/2020. Before data collection, informed consent was obtained from each participant. All ethical considerations, such as confidentiality and privacy, were considered.

3. Result

3.1. Sociodemographic characteristics of T2DM patients

A total of 407 T2DM patients were enrolled in this study, with men accounting for the majority (54.05%) of the participants. The age of the participants ranged from 20 to 50 years old. The majority of study participants (61.7%) were city dwellers, and more than two-thirds (68.3%) were married. About 28.8% and 34.2% of study participants were government employees and were unable to read and write, respectively (Table 1).

3.2. Life style and clinical characteristics

The majority of study participants did not take naps (68.8%), eat dinner after 8:00 p.m. (71.7%), exercise (70.5%), or follow a balanced diet (86%) as recommended by their doctor (Table 2). From the total respondents, 55.3% of the study participants had lived less than seven years after being diagnosed with DM. The majority of the study participants had no family history of diabetes (73.5%), no DM complications (65.4%), were non-hypertensive (62.9%), and were highly adherent to their medication (75.92%). Metformin was taken by approximately 43.5% of study participants. Regarding the anthropometric measure, the majority of the study participants had a normal BMI (58%). They had a low risk of having a large waist circumference (50.9%). (Table 2).

About 53.1% of the study participants had a moderate risk of OSA (Fig. 1).

3.3. Prevalence of poor glycemic control

The study participants' median FBG level was 189.67105 mg/dl (interquartile range). The overall magnitude of poor glycemic control was 54.1% (95% CI: 49.2%–58.9%). It was higher among females (60.4%), rural dwellers (60.3%), participants who were unable to read and write (63.31%), and divorced individuals (72.5%) (Table 3).

3.4. Factors associated with poor glycemic control

Low and intermediate risk of OSA were identified as factors

Table 3
The magnitude of poor glycemic control among T2DM patients attending at in Felege Hiwot Comprehensive Referral and Specialized Hospital,Northwest Ethiopia, 2021.

Variables	Categories	Glycemic control		Chi-square test
		Good (%)	Poor (%)	
Sex	Male	113 (51.36)	107 (48.64)	0.017
	Female	74 (39.57)	113 (60.43)	
Residence	Rural	62 (39.74)	94 (60.26)	0.048
	Urban	125 (49.80)	126 (50.20)	
Education status	not read and write	51 (36.69)	88 (63.31)	0.012
	Primary	36 (42.35)	49 (57.65)	
	Secondary	42 (56.00)	33 (44.00)	
	College and above	58 (53.70)	50 (46.3)	
Occupational status	Farmer	23 (32.86)	47 (67.14)	0.059
	Merchant	18 (46.15)	21(53.85)	
	Government employ	64 (54.70)	53 (45.30)	
	Self-employed	29 (53.70)	25 (46.30)	
	Housewife	35 (41.67)	49 (58.33)	
	Jobless	18 (41.86)	25 (58.14)	
Sleep quality	Good	170 (63.20)	99 (36.80)	P < 0.01
	Poor	17 (12.32)	121 (87.68)	
OSA	Low risk	144 (66.67)	72 (33.33)	P < 0.01
	Intermediate risk	30 (35.29)	55 (64.71)	
	High risk	13 (12.26)	93 (87.74)	
Sleep duration	<6 h.	11 (8.94)	112 (91.06)	P < 0.01
	6–8 h.	151 (70.56)	63 (29.44)	
	>8 h.	25 (35.71)	45 (64.29)	
Type of medication	Insulin	80 (50.31)	79 (49.69)	P < 0.01
	Metformin	90 (50.85)	87 (49.15)	
	Insulin and metformin	17 (23.94)	54 (76.06)	

associated with poor glycemic control in primarily female individuals. The odds of poor glycemic control are 2.7 times (AOR = 2.7, 95% CI: 1.23–6.15) higher among females compared to males. T2DM patients who had poor sleep quality had a 3.3-fold (AOR = 3.3, 95% CI (1.16, 9.37) higher chance of poor glycemic control than patients who had good sleep quality. The odds of having poor glycemic control among T2DM patients who were at low or intermediate risk of OSA were decreased by 97% (AOR = 0.03, 95% CI: 0.01, 0.12) and 85% (AOR = 0.14, 95% CI: 0.05, 0.43), respectively, compared to T2DM patients who were at high risk of OSA. T2DM patients with short sleep duration had an 8.3 times (AOR = 8.3, 95% CI: 2.66–25.85) higher risk of poor glycemic control, while those with long sleep duration had a 2.6 times (AOR = 2.6, 95% CI: 1.12–6.04) higher risk of poor glycemic control (Table 4).

4. Discussion

In this study, The poor glycemic control in T2DM patients was found to be high. Being female, poor sleep quality, both short and long sleep duration, intermediate and low risk of obstructive sleep apnea, and poor adherence to the diet recommended by the physician were statistically associated with poor glycemic control.

In the present study, the magnitude of poor glycemic control was 54. This finding is consistent with a study conducted in Nigeria (55%) [16]. On the other hand, the results of the present study are lower than those studies conducted in India (74%) [17], Malaysia (72%) [18], Cameron [19] and Kenya (83%) [10]. On the other hand, the finding of the current study is higher than that of a study conducted in the United States of America (12.9%) [4]. This discrepancy could be due to the effect of industrialization, provision of electricity, and urbanization that results in longer working hours, more shift work, and 24-h availability of commodities [20]. These services and activities may have an impact on people's sleep duration and quality which has a consequence on glycemic control. The implementation of national sleep foundation standards in the management of diabetes in their hospitals could explain this discrepancy.

In this poor glycemic control was significantly associated with the female sex hich is supported by a study conducted in Tanzania [21] however, contradicts the findings from China, Malaysia, and Jordan [4, 22]. This disparity could be attributed to the fact that females in Ethiopia and other poor nations face a greater burden than those in developed countries. The plausible mechanism could be also due to insulin resistance that comes after menopause. Studies have reported that diabetic women are more likely to lose glucose homeostasis after menopause [23]. The other possibility is the proportion of testosterone in the body. Because testosterone stimulates lipolysis in adipose tissues, low testosterone levels are associated with abdominal obesity and insulin resistance in females [24]. Another study also reported that metformin has a better effect on glucose metabolism in type 2 diabetic males than in females [25].

In this study, T2DM patients who have poor sleep quality have poor glycemic control levels. This is also supported by another study [26].

Another factor that was significantly associated with poor glycemic control in this study was short sleep duration (<6 h). This is supported by research conducted in Brazil and Japan [27]. Long sleep duration (>8 h) was also associated with poor glycemic control in this study. These findings are similar to studies conducted in Japan [28] and China [29]. The best sleep duration which helps to have good glycemic control is 6–8 h.

In general, sleep pattern has a major modulatory effect on glucose metabolism and energy uptake that have a direct or indirect effect on the maintenance of good glycemic control level in T2DM patients. Furthermore, the increased prevalence of poor glycemic control levels with sleep deprivation and/or poor sleep quality could be due to upregulation of appetite, increased time for eating as well as reduced energy expenditure. Indeed, nocturnal awakening and arousal have been associated with altered leptin levels and leptin resistance leading to dysregulation of the hypothalamic-pituitary-adrenal axis, resulting in glucose metabolism impairment [29].

Sleep deprivation stimulates the cerebral cortex, cerebral-limbic system and hypothalamus, which induces the secretion of catecholamines from the sympathetic ganglion and adrenal medulla and cortisol from the pituitary-adrenal system. These hormones function to increase the plasma glucose level and cause high insulin resistance.

The other plausible mechanism related to sleep deprivation is the disturbance of melatonin hormone secretion under the control of the hypothalamic suprachiasmatic nucleus (SCN). This hormone or its receptor agonist's administration improved glucose homeostasis through, enhanced glucose uptake, increased glucose-induced insulin secretion, improved insulin sensitivity and decreased liver gluconeogenesis, and also increase glycogen synthesis in the liver. In the normal sleep-wake-

Table 4
Factors associated with poor glycemic control among T2DM patients attending at in Felege Hiwot Comprehensive Referral and Specialized Hospital,Northwest Ethiopia, 2021.

Variable	Glycemic control		Bivariable analysis			Multivariable analysis		
	Good (187) frequency (%)	Poor (220) frequency (%)	p-value	COR	(95% CI)		AOR	(95% CI)
Sex								
Male	113 (51.4)	107 (48.6)		1			1	
Female	74 (39.6)	113 (60.4)	0.02	1.6	1.1,2.4	**0.014**	**2.75**	**1.2,6.2***
Sleep Quality								
Good	170 (63.2)	99 (36.8)		1			1	
Poor	17 (12.3)	121 (87.7)	0.00	12.2	6.94,21.50	**0.025**	**3.30**	**1.16,9.37***
OSA								
Low risk of OSA	144 (66.70)	72 (33.30)	0.00	0.07	0.04,0.13	**0.000**	**0.04**	**0.01,0.12**
Intermediate risk of OSA	30 (35.30)	55 (64.70)	0.00	0.26	0.12,0.53	**0.001**	**0.14**	**0.05,0.43**
High risk of OSA	13 (12.26)	93 (87.74)		1			1	
Sleep duration								
6–8 h.	151 (70.6)	63 (29.4)		1			1	
<6 h	11 (8.9)	112 (91.1)	0.00	24.4	12.29,48.44	**0.000**	**8.3**	**2.66,25.85**
>8 h.	25 (35.7)	45 (64.3)	0.00	4.3	2.44,7.63	**0.026**	**2.61**	**1.12,6.04**

Note: CI = confidence interval, COR = crude odds ratio, AOR = adjusted odds ratio, OSA = obstructive sleep apnea, hr. = hour; $P < 0.05$.

up cycle this hormone is secreted in the pineal gland under the control of the hypothalamic suprachiasmatic nucleus and detected in liver, fat, muscle, and pancreas cells to aid glucose homeostasis [30].

In this study, both low and intermediate risk of obstructive sleep apnea were significantly low risk of h poor glycemic control. This is in line with a study conducted in India [31].

Studies have demonstrated that intermittent hypoxia or OSA syndromes can induce liver damage and increase serum levels and activity of key liver enzymes such as serum aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase in both mice and humans [32]. Repeated attacks of OSA resulted in liver steatosis, necrosis, and inflammation with neutrophil accumulation and collagen deposits. This causes glucose homeostasis abnormalities even in T2DM patients. OSA syndrome can also cause oxidative stress and inflammation that results in the secretion of inflammation mediators [33].

In this study balanced diet recommended by the physician is another independent variable that significantly associated with poor glycemic control. T2DM patients who are not on the diet recommended by their physician are more likely susceptible to develop poor glycemic control.

Add one paragragh about limitation and strength of this study.

5. Conclusion

The extent of poor glycemic control in T2DM patients was significant. Being female, having poor sleep quality, and sleeping for short or long periods were all statistically significant factors associated with poor glycemic control. Thus, to enhance glycemic control and prevent complications in T2DM patients, healthy sleep habits are recommended. DM patients for the presence of obstructive sleep apnea should be assessed and treat them accordingly. Successive researchers should focus on measuring glycemic control level by using HbA1C and try to measure sleep quality by using object sleep measurement tools line actigraphy and polysomnography.

Availability of data and materials

The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the manuscript.

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CRediT authorship contribution statement

Yadelew Yimer Shibabaw: are equally involved in conception, Methodology, execution, Funding acquisition, acquisition of data, Formal analysis, analysis and interpretation, Writing – original draft, drafting and critically reviewing the paper, and. **Tadesse Asmamaw Dejenie:** are equally involved in conception, Methodology, execution, Funding acquisition, acquisition of data, Formal analysis, analysis and interpretation, Writing – original draft, drafting and critically reviewing the paper. **Kibur Hunie Tesfa:** involved during searching literature, Writing – original draft, drafting and critical reviewing of the paper.

Declaration of competing interest

The authors declare that they have no competing interests.

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Abbreviations:

ADA	American Diabetic Association
DM	Diabetes Mellitus
FBG	Fasting Blood Glucose
HbA1C	Glycosylated Hemoglobin A1C
FHCRSH	Felege Hiwot Comprehensive Referral and Specialized Hospital
OSA	Obstructive Sleep Apnea
PSQI	-Pittsburg Sleep Quality Index
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
USA-	United States of America

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