DETERMINING SLEEP-WAKE ACTIVITY USING ACTIWATCH IN HEALTHY ADULTS AND TYPE 2 DIABETES

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Abstract: Aims: Metabolic disorder (MD) such as type 2 diabetes mellitus (T2DM), hypertension and other cardiovascular diseases could lead to sleep disturbance. The aim of the present study is to determine the relationship between quality and duration of sleep with or without hypertension in type 2 diabetes adults using actigraphy.
Methods: A total of 23 subjects were allowed to wore Actiwatch, for seven days time period. Sleep parameters (total sleep time (TST), sleep onset latency and sleep efficiency (SE)) were recorded with the help of actigraphy report. Systolic and diastolic blood pressure were measured, hbA1c and lipid profile value were also measured in type 2 diabetic patients.
Results: On comparison of sleep duration among the two groups of individuals, diabetic and non-diabetic, there was significant difference found in the sleep-wake activity. TST (hrs) with the (p-value = 0.014) and Wake After Sleep Onset (WASO) (min) (p-value = 0.001). In individuals with sleep duration of less than 5 hours, MDs were found and were subjected to pharmacological treatment.
Conclusions: It is concluded by the above study that MD such as diabetes, hypertension and other cardiovascular diseases, uncontrolled glycemic control affects the duration and quality of sleep. Actigraphy can play a significant role in monitoring daily activity and can asset in maintaining a healthy lifestyle.

Keywords- Actiwatch, glycemic control, sleep parameters, sleep onset latency, sleep efficiency, systolic and diastolic blood pressure

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INTRODUCTION:

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder (MD) in which the beta cells do not produce a required amount of insulin and/or there is insulin resistance [1]. Impaired insulin secretion and increased insulin resistance, together contribute to the development of this disease as type 2 diabetes is a progressive disease as functional pancreatic cell mass reduces over time [2]. In the pathogenesis of the T2DM, it is considered that the insulin resistance plays an important role [3] both insulin secretion [4], and action [5] are inhibited in chronic hyperinsulinemia. Insulin resistance is found in hypertension, hyperlipidemia, and ischemic heart disease, entities commonly found in association with diabetes insulin resistance are found in hypertension [6-8].

According to the 2017 International Diabetes Federation's Diabetes Atlas, it has been reported that 425 million adults worldwide have the burden of this chronic disease it means one in 11 adults is affected by this MD, among which t2dm is the common one[9]. The incidence of t2dm patients is found higher; with over 80% of people in low-to-middle-income countries, though the incidence and prevalence of t2dm vary geographically [10], the prevalence of t2dm has increased worldwide since 1980 [11]. At present India has the burden of ~70 million diabetes population [12]. Apart from this classical view, today we know that there is at least 15 more Pathophysiology known to complicate the metabolic mechanisms of diabetes. It has been found from many previous studies that T2DM affects every organ of the body [13,14]. The other organs involved include brain, liver, gut, kidney and adipose tissue. We have enough number of oral hypoglycemic agents, to manage hyperglycemia apart from the injectable insulin and glucagon-like peptide 1 receptor (GLP-1) agonists; still the management of diabetes is not satisfactory leading to serious complications including compromised sleep problems.

Insulin resistance is found in hypertension in association with diabetes [6]. Cardiovascular diseases are among one of the major risk factors in t2dm subjects [15-18]. It is generally found that diabetic patients are prone to silent heart attacks and are more prone to the formation of blood clots [19]. A number of studies have revealed that sleep disorder (SD) is an autonomous risk factor for hypertension, cardiovascular disease (CVD) [17, 20-23], and impaired glucose metabolism [24]. Snoring, a common symptom of SD is independently associated with impaired glucose tolerance and t2dm [25, 26]. Various studies have suggested that approximately 40% of patients with obstructive sleep apnoea (OSA) have t2dm [27]. The prevalence of OSA in patients with t2dm is estimated up to 23% [28].

Altered or impaired glucose metabolism and cardiovascular disease, hypertension leads to (SDs) such as sleep deprivation, sleep disordered breathing including several types of sleep apnoea, snoring, upper airway resistance syndrome etc [29]. Studies have also been believed that there is some relation between diabetes mellitus and SD [30-31, 23]. Till date, the defined mechanism behind the relationship between diabetes mellitus and SD are not well implicated. It has been reported that chronic intermittent or episodic hypoxia and sleep fragmentation lead to a number of pathogenic factors such as increased sympathetic activity, dysregulation of the hypothalamus-pituitary-adrenal axis, and activation of inflammatory pathways, resulting in abnormal glucose metabolism [29,17]. Major risk factors for hypertension and type 2 diabetes mellitus are somewhat similar from many aspects, including family history, sedentary lifestyle, cigarette smoking, poor and unhealthy diet and one of the important factor is poor sleep which is often overlooked most of the time [32]. It has been demonstrated by researchers that there is some link between poor quality of sleep and its adverse effect on health [33, 34]. Diabetes and hypertension coexist and shares a common pathway as revealed by several studies [35-37]. Hypertension is a condition often present in type 2 diabetes mellitus. SD is one of the most common factors determined in adults with hypertension and type 2 diabetes mellitus [38]. Here, we have used actigraphy i.e. actiwatch to determine quality and quantity of sleep in people with t2dm in comparison with healthy adults or controls.

METHODS AND PROCEDURES:

*Selection of Cases***:**

Twenty-three adults men and women between the ages 21 and 60 years were selected among which twelve adults were having diabetes i.e. type 2 diabetes mellitus and rest were healthy individuals or controls that had taken part for the present study. They attended the Department of Physiology, King George's Medical University, Lucknow, U.P. India. The subjects were enrolled for the study from the time period of 20/01/2016 to 17/08/2017. All subjects were in good physical and mental health. None of the individuals with diabetes used insulin injection. They were all nonsmokers, and individuals none consumed any drugs or medications that could affect sleep. Participants were excluded for the presence of sleep disturbances such as sleep complaints, sleep apneas, and hypopneas. All subjects signed a consent form that informed them of the nature and risks of the study.

Table 1 Characteristics of subjects involved in the present study

Age, y	41.35±01
BMI, kg/m²	22.2±01
Duration of diabetes, y	12.3±01
Hba1c (t2dm), % (mmol/mol)	6.20±00
BP,mmHg Systolic	132±02
Diastolic	80.8±01
Lipid profile (t2dm), mg/dL Serum cholesterol	159±02
Triglyceride	165±02
HDL	46.7±01
LDL	77.8±01
VLDL	33.1±01

Mean values

BMI: Body Mass Index, HbA1c: glycated haemoglobin, BP: Blood Pressure, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low density lipoprotein

Procedures

All twenty-three subjects were given an actiwatch (Actiwatch-2 Philips Respironics) to wore on the wrist of the left hand with the base of the instrument positioned against the inside of the wrist, below the thumb, for seven days of time period. Sleep parameters (total sleep hours, sleep onset latency and sleep efficiency) were recorded with the help of actigraphy report. Systolic and diastolic blood pressure were measured in controls and subjects. HbA1c (glycated hemoglobin) and lipid profile value were also measured in T2DM patients.

MEASURES

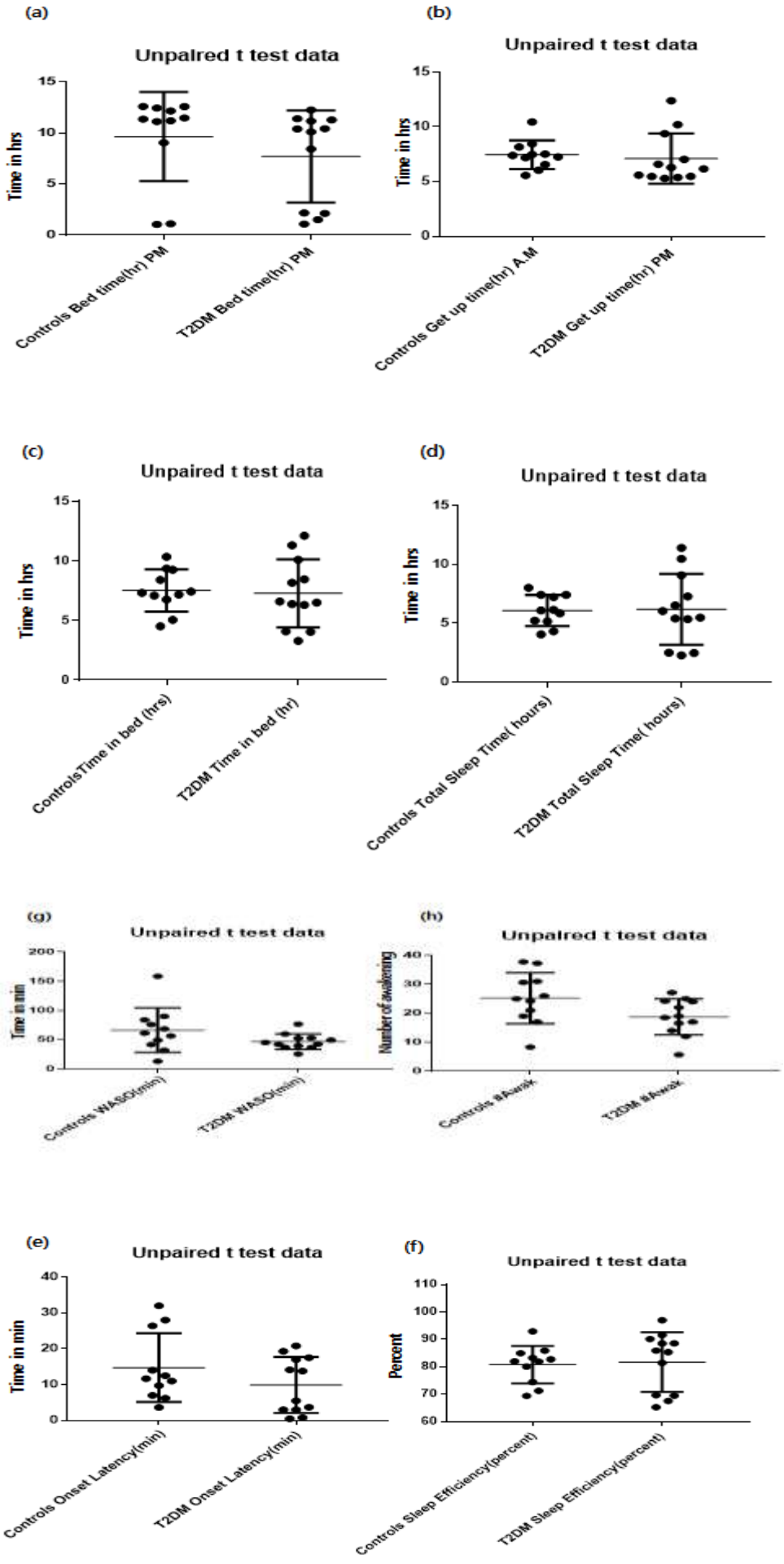
Actigraphy Daily activity and sleep/wake pattern were recorded using an Actiwatch-2 (Respironics). This small, watch-like device contains an accelerometer that senses and records physical motion in all directions and a photodiode to monitor light intensity. Motion is converted to an electric signal and digitally integrated to derive an activity count. Sensitivity is 0.025 G (a 2 count level), with a bandwidth between 0.35 - 7.5 Hz typical and a sampling rate of 32 Hz. The 0.35 - 7.5 Hz bandwidth used in the Actiwatch monitor is higher and larger than in other commercially available actigraphs (0.25-3 Hz). Data were averaged by the monitor into one-minute epochs. After monitoring, the data were downloaded onto a computer to an Actireader via a wireless link set up by Actiware 2.0 [39]. All sleep episodes were visually inspected before analysis to screen for artifacts and malfunctioning.

STATISTICAL ANALYSIS

Results were analyzed statistically between groups (t2dm patients and controls) by using graph pad prism (GraphPad software, inc.) software. Data are presented as the mean ± standard error of the mean (SEM), and means were compared with two-tailed unpaired student t-test or one-way analysis of variance (SEM). Statistical significance was attained when p values were <0.05, with the confidence interval 95%.

RESULTS

An unpaired t-test data analysis explores the outcome Mean ± SEM in **Table 2**, for all the sleep parameters recorded by actidata in all the 23 subjects. As indicated in **Table 2**, positive and strong correlation can be observed in total sleep time (TST) measured in hours (hrs) among controls and subjects with the (p-value = 0.014) and in wake after sleep onset (WASO) measuring unit minutes (min) (p-value = 0.001). As shown in **Figure1** the graphs indicated the difference between the two groups of individuals taken part in sleep/wake activity for


(a)
Unpaired t test data
Time in hrs
Controls Bed time(hr) PM
T2DM Bed time(hr) PM
(b)
Unpaired t test data
Time in hrs
Controls Get up time(hr) A.M
T2DM Get up time(hr) PM
(c)
Unpaired t test data
Time in hrs
ControlsTime in bed (hrs)
T2DM Time in bed (hr)
(d)
Unpaired t test data
Time in hrs
Controls Total Sleep Time(hours)
T2DM Total Sleep Time(hours)
(g)
Unpaired t test data
Time in min
Controls WASO(min)
T2DM WASO(min)
(h)
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Number of awakening
Controls #Awak
T2DM #Awak
(e)
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Time in min
Controls Onset Latency(min)
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(f)
Unpaired t test data
Percent
Controls Sleep Efficiency(percent)
T2DM Sleep Efficiency(percent)

Figure 1: a. bedtime in hours P.M. control vs t2dm **b**. get up time in hours A.M. control vs t2dm **c**. time in bed in hours control vs t2dm **d**. total sleep time in hours control vs t2dm **e.** Onset latency in minutes control vs t2dm **f**. sleep efficiency percent control vs t2dm **g**. WASO (wake after sleep onset) in minutes control vs t2dm **h**. #awake control vs t2dm

Table 2- Description of the findings with all the sleep parameters produced by actiwatch.

N =21	Controls	Subjects	Difference between means	p-value
Bed time(hr)	9.646 ± 1.31	37.693 ± 1.303	-1.953 ± 1.852	0.917
Get up time(hr)	7.464 ± 0.393	7.106 ± 0.665	-0.357 ± 0.791	0.083
Time in bed (hr)	7.521 ± 0.532	7.281 ± 0.820	-0.240 ± 0.998	0.144
Total Sleep Time (hr)	6.072 ± 0.399	6.18 ± 0.871	0.108 ± 0.988	0.014
Onset Latency(min)	14.75 ± 2.89	9.931 ± 2.257	-4.822 ± 3.634	0.513
Sleep Efficiency	80.86 ± 2.056	81.76 ± 3.126	0.901 ± 3.816	0.156
WASO(min)	66.48 ± 11.48	46.72 ± 3.789	-19.76 ± 11.66	0.001
#Awak	25.21 ± 2.657	18.76 ± 1.794	-6.45 ± 3.157	0.267

(Mean ± SEM, 95% confidence interval, P < 0.05)

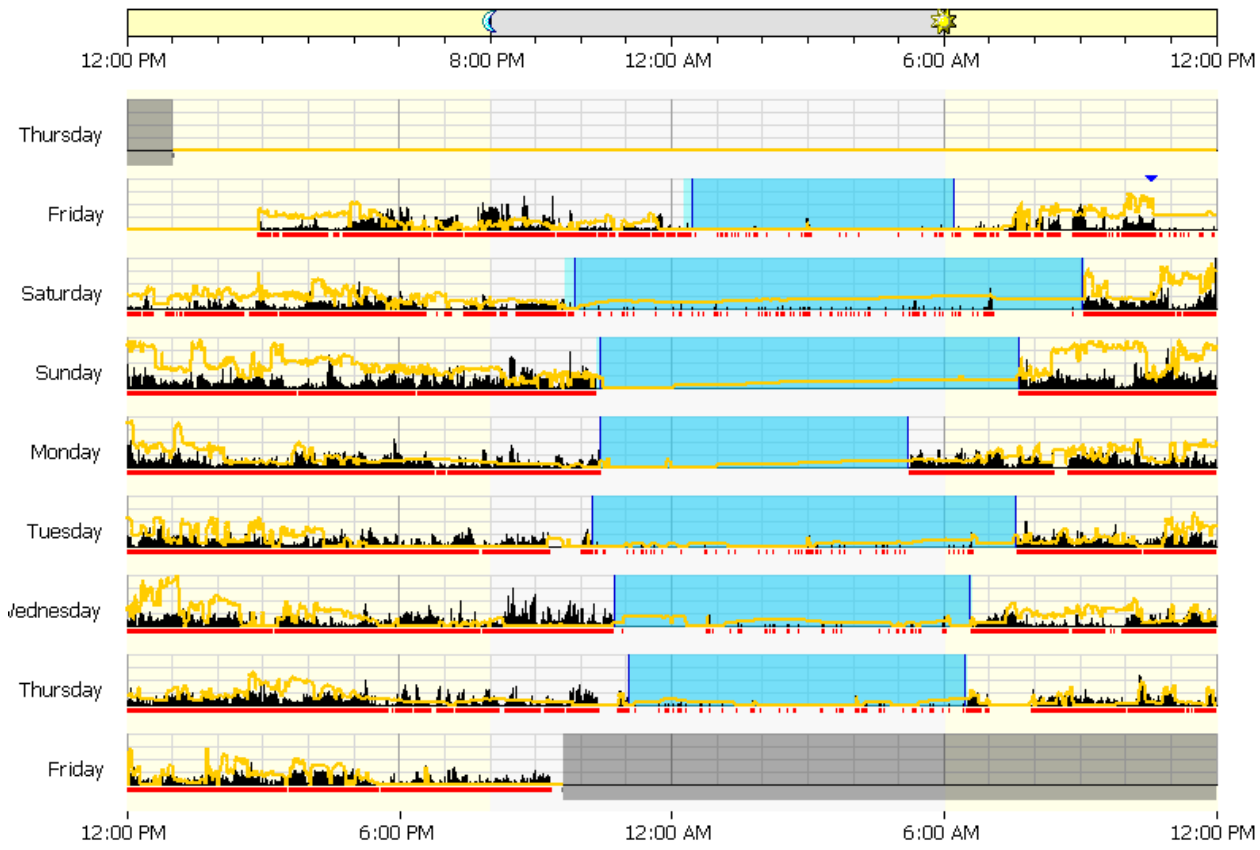

Figure 2 : Example of the actogram/graph report measured on one person for seven days time period.

An actogram shown in **Figure 2** also known as raster plot, it's a graphic representation of the distribution of rest and activity periods for a subject throughout the day. Strip chart indicates the individual 24-hour periods, they are stacked one above the other, to make the evident the sleep/wake patterns across multiple days. Black lines indicate activity data, sleep/wake scores are shown below activity. Red indicates wake. White indicates sleep. Excluded intervals are represented by dark blue shading. Rest periods are represented by blue shading, sleep intervals are represented by grey shading. Grey shading represents invalid data interval.

DISCUSSION

The present study examined the sleep-wake activity on healthy adults and type 2 diabetes subjects using an accelerometry device designed to measure activity and sleep- wake behaviours. We evaluated the sleep parameters among two groups of individuals, as well as the comparability of data from actigraphy device in above mentioned two groups of individuals. We specifically examined how the sleep parameters generated by actiwatch compared to reference standards. The results showed that an accelerometry device designed specifically to assess sleep-wake activity provide measures of sleep duration and also represents the level of activity time spend in light and dark during the day and night. We also observed variability in total sleep time estimates derived from the two groups taken part in the study.

The actiwatch device is used to better understand the daily sleep-wake pattern in individuals. Actigraphy principle is used in actiwatch to produce sleep schedule variability, sleep quantity and sleep quality statistic, apart from it, a highly sensitive accelerometer is equipped in it which helps in measuring total sleeping period, wake after sleep onset, and sleep efficiency in free-living condition[39]. Wrist actigraphy provides accurate data collection, and precise data analysis, and objective measurements of motion that can be used to quantify daily activity and sleep quality [40]. In the present study, two groups of individuals healthy adults and subjects with metabolic disorder specially with type 2 diabetes exhibited strong correlations with the sleep parameter in analyses of total sleep time. The association between sleep-related disorders and incident diabetes has been examined only in a few studies, so far most of the studies are dealing with sleep disturbance and risk of diabetes in future. SD is often observed in subjects with diabetes [41]. Sleep loss and sleep disturbances could lead to the development of insulin resistance and Type 2 diabetes either directly by having a deleterious effect on components of glucose regulation or indirectly via a dysregulation of appetite, leading to weight gain and obesity, a major risk factor for insulin resistance and diabetes [2] both-cell responsiveness and insulin sensitivity are influenced by sleep.

It is found that both the short and long duration of sleep was associated with type 2 diabetes [42]. Subjects with type 2 diabetes showed significant difference in TST in the present study. Human sleep is generally consolidated in a single 7- to 9-h period, and therefore an extended period of fasting must be maintained overnight. In normal subjects, during overnight sleep, blood levels of glucose remain stable or fall only minimally despite the extended fast [43]. Our results also estimated the role of WASO, as it is an important tool for measuring sleep quality. Measures of WASO in this sample significantly correlated between the two groups. WASO is a measure of the time spent awake after first falling asleep. It has been clear through our result that quality of sleep is affected in subjects with metabolic disorder.

A limitation of this study is the small sample size of both the groups controls and subjects. Future work should include greater sample size with different metabolic diseases such as obesity, type 2 diabetes, hypertension and other cardiovascular diseases, as well as expand assessment. The study was also limited to the group of people involved for the study, only a trusted well known people were allowed to wore actiwatch. And the diabetic individuals blood glucose levels were in range below with no complications of sleep.

The study's strengths include concurrent data collection from actigraphy device with controlled evaluation that allowed the performance of the device to be assessed without environmental influences.

CONCLUSIONS

The sleep-wake activity determined in two groups of individuals, healthy adults and type 2 diabetes subjects with the help of actigraphy device produced reliable measures and appears to have the beneficial effect in the diagnosis of any disturbance in sleep-wake activity affected by metabolic diseases or disturbance in sleep-wake activity could affect metabolism. Further, we were able to show the effect of metabolic disease type 2 diabetes on the sleep-wake activity. Though, the subjects involved in the study do not have any moderate to major complications caused by type 2 diabetes and hypertension. Further research should involve subjects with moderate to major complications so that a better understanding could be assessed.

ABBREVIATIONS

SE	Sleep Efficiency
HbA1c	glycatedhemoglobin
TST	total sleep time
WASO	wake after sleep onset
MD	metabolic disorder
T2DM	Type 2 diabetes mellitus
GLP-1	glucagon-like peptide 1
SD	sleep disorders
CVD	cardiovascular disease
OSA	obstructive sleep apnoea
SEM	standard error of the mean

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Institution of Performed Work

The present study was conducted in the Department of Physiology, King George's Medical University, Lucknow, India.

Disclosure Statement

This was not an industry support study. Dr.NarsinghVerma has received the equipment from Philips Respironics for use in clinical trials.All authors have seen and approved the manuscript. The authors report no financial conflicts of interest.

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