

The Influence and Treatment of Sleep Disorders on Diabetes Mellitus

Xiaohan Sun

*Georgia State University, Atlanta, USA
xsun21@student.gsu.edu*

Abstract: Sleep disorders and diabetes mellitus are both prevalent and increasingly common chronic diseases that significantly impact public health. Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia due to defective insulin secretion or action, leading to multi-system complications. Notably, sleep disorders—including obstructive sleep apnea (OSA), insomnia, and restless legs syndrome (RLS)—are highly prevalent in diabetic populations and often worsen glycemic dysregulation. Sleep disorders impair insulin sensitivity, trigger neuroinflammation and oxidative stress, and disrupt glucose metabolism, thereby worsening insulin resistance and hyperglycemia. Furthermore, alterations in circadian rhythms and reduced sleep quality compromise endocrine and metabolic balance, creating a vicious cycle that hinders effective diabetes control. This article explores the complex and bidirectional relationship between sleep disturbances and diabetes mellitus, emphasizing how disrupted sleep contributes to the development, progression, and poor control of diabetes. It also examines how diabetes-related complications, such as autonomic neuropathy and nocturnal polyuria, further worsen sleep quality. Current treatment strategies, including continuous positive airway pressure (CPAP) therapy for OSA, pharmacological interventions, and behavioral therapies, are discussed. The article highlights the importance of a multidisciplinary approach integrating sleep assessment with diabetes care to enhance clinical outcomes and overall quality of life.

Keywords: Sleep disorder, Diabetes mellitus, Circadian rhythms

1. Introduction

Diabetes mellitus is a prevalent chronic disease demanding lifelong glycemic control through sustained medical management. According to the statistics from the International Diabetes Federation, by the end of 2025, more than 500 million people in the world will have diabetes mellitus, and the number is still growing. While diabetes patients are primarily middle-aged and elderly people, the number of young people and children is also increasing, mainly due to obesity and unhealthy lifestyle habits. Among these, sleep disorders are a significant concern. Previous studies indicate that the incidence of sleep disorders among diabetics is as high as 50%~70%, which is always associated with the onset of different diseases [1]. Moreover, sleep disorders exacerbate challenges for diabetes patients in the regulation of blood sugar, including conditions such as Obstructive Sleep Apnea (OSA), sympathetic nervous system dysfunction, and diabetic neuropathy. For example, OSA leads to intermittent hypoxia and overactivation of the sympathetic nervous system, which increases insulin

resistance and worsens diabetes. Its main symptoms are snoring during sleep, holding breath at night, daytime lethargy, frequent awakening at night, headache, and lack of concentration.

Sympathetic nervous system (SNS) overactivation disrupts deep sleep by increasing nighttime awakenings. It is also a hallmark of diabetic autonomic neuropathy. Patients with SNS may experience nighttime heart rate acceleration that easily wakes them up. Many patients also feel leg pain and burning sensations at night, further impairing sleep quality. These mechanisms illustrate how sleep disorders worsen diabetes outcomes. Nevertheless, sleep disorders directly impair blood sugar control by affecting the metabolism and function of insulin, resulting in erratic blood glucose fluctuation. Insulin is the key hormone that regulates blood sugar. Insulin resistance prevents the body from using blood sugar effectively, resulting in hyperglycemia. Conversely, high blood sugar will further affect the central nervous system, increasing sympathetic activity and causing fragmented sleep. In addition, sleep disorders can also affect the secretion of various hormones. In particular, sleep disorders will lead to a reduction or disorder of the growth hormone secretion, which will lead to the slow growth of young people with diabetes and affect their health and development [2]. Meanwhile, both excessive and deficient levels of growth hormone can affect the stability of blood glucose control. Additionally, it also will elevate the levels of cortisol, which stimulates glucose production and inhibits the level of insulin, exacerbating metabolic dysfunction. Finally, sleep disorders amplify inflammation. Diabetes is a chronic inflammatory disease with a high level of blood sugar. It will activate the immune system and produce a variety of inflammatory factors such as TNF- α , IL-6, and CRP. Inflammatory factors can interfere with brain sleep regulation, especially the hypothalamic-brain stem network, resulting in shortened sleep time, deep sleep reduction, and a decline in the quality of sleep. Also, it has a relationship with the OSA. After inflammation is activated, it will lead to the intensification of insulin resistance, forming a vicious circle of diabetes and OSA [3-5]. Therefore, it is important for the diabetic patients to control the blood sugar and prevent complications related to diabetes. This review aims to elucidate the relationship between sleep disorders and diabetes mellitus, hoping to fully understand the adverse effects of sleep disorders and help develop targeted interventions for diabetes.

2. The influence of sleep disorders on diabetes

In daily life, there are many sleep-related diseases that can impair the blood sugar control in patients with diabetes. OSA is a disease caused by recurrent collapse and obstruction of the upper respiratory tract during sleep, which may or may not involve decreased oxygen saturation. During REM sleep, the reduced muscle activity and decreased tension in the upper airway make it more prone to collapse. These obstructions can lead to awakenings, oxygen destruction, or both, causing fragmented sleep. The repeated respiratory pauses and blood oxygen fluctuations caused by OSA overactivated the sympathetic nervous system, triggering the release of neurotransmitters and hormones such as catecholamines, including epinephrine. This stimulates the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased cortisol secretion. Intermittent hypoxia also can lead to oxidative stress, promote the release of pro-inflammatory cytokines, and further elevate cortisol levels. Among them, catecholamines directly act on insulin beta cells, reducing insulin secretion. Cortisol not only inhibits the function of pancreatic beta cells and reduces insulin secretion but also weakens the cellular response to insulin by reducing the sensitivity of insulin receptors, leading to insulin resistance. OSA can also trigger the release of inflammatory factors, contributing to chronic systemic inflammation. Specifically, TNF- α and IL-6 are released in large quantities from adipose tissue, monocytes, and phagocytes. These cytokines can directly interfere with insulin receptor signaling, further reducing the sensitivity and exacerbating the elevated blood sugar levels. Additionally, numerous studies indicate a significant association between OSA and the incidence of type 2 diabetes. Some studies suggest that this relationship only exists in patients with moderate to severe OSA. Patients with severe

OSA exhibit a 2-3-fold increased risk of developing diabetes compared to the general population. Conversely, OSA prevalence among individuals with type 2 diabetes ranges from 15% to 30%. There is a strong correlation between increasing OSA severity and elevated HbA1c levels, which are typically 0.5%-1% higher than those of the general population, indicating chronic hyperglycemia. Compared to mild or no OSA, severe OSA may lead to a 0.5%-0.8% increase in HbA1c after adjusting for confounding factors [6, 7]. However, there is currently no data demonstrating its occurrence in moderate and severe cases.

Insomnia is a prevalent sleep disorder clinically defined by persistent difficulties with sleep initiation, maintenance, or early morning awakenings. Approximately 15% of U.S. adults suffer from insomnia, but the rate is even higher among type 2 diabetes patients. The World Health Organization (WHO) reports that sleep disorders affect an estimated 27% of the global population, representing a significant public health concern. Women are 1.5 times more likely to develop insomnia than men, and its prevalence increases with age, particularly affecting middle-aged and elderly patients with diabetes [6]. Insufficient sleep contributes to insulin resistance and impaired glucose tolerance, increasing the risk of type 2 diabetes. The persistent activation of the sympathetic nervous system leads to elevated levels of adrenaline and noradrenaline. These hormones suppress insulin secretion while stimulating hepatic glucose release, resulting in hyperglycemia and contributing to the pathogenesis of insulin resistance. Experimental studies demonstrate that insomnia increases the likelihood of elevated glycosylated hemoglobin levels. Chronically high HbA1c can lead to reduced vision and even blindness due to diabetic retinopathy. It can also cause nerve damage, triggering diabetic peripheral neuropathy, which may result in numbness, tingling, or loss of sensation in the hands and feet. In addition, short sleep duration is an important but modifiable risk factor for obesity. The Quebec family study, which assessed obesity and leptin levels, found that individuals who slept for 7-8 hours had a lower risk of obesity compared to those who slept only 5-6 hours. Meanwhile, the study also revealed a strong association between short sleep duration and reduced levels of leptin. After adjusting for plasma leptin levels, the differences in obesity rates between individuals with short and normal individuals became insignificant. This finding suggests that leptin acts as a key mediator in the relationship between sleep duration and obesity.

With the development of modern society, diabetes patients are becoming increasingly younger and younger, which is inseparable from their daily lifestyle. Among these, the circadian rhythm disruption is one of the key contributors [2]. The circadian rhythm system allows organisms to synchronize with Earth's 24-hour light-dark cycles. In mammals, this system comprises a hierarchical organization: a central pacemaker in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus and peripheral oscillators distributed across most tissues. These rhythms align with the precise 24-hour environmental cycle by relying on external cues. The most important cue for the central pacemaker in the SCN is the light input received through the eyes. This light signal is directly transmitted from intrinsically photoreceptor retinal ganglion cells (ipRGCs) to the SCN via the retinohypothalamic tract. After that, the SCN synchronizes the peripheral clock through neurons and endocrine signals, ensuring that the circadian rhythm remains aligned with the external environment. This synchronization is crucial for maintaining optimal homeostasis in endogenous metabolic processes. Disruptions to this equilibrium can affect numerous physiological rhythms, including hormone release and energy metabolism. Clinical evidence demonstrates that sleep deprivation elevates heart rate, cortisol secretion, and 3-methyladrenaline levels, reflecting concurrent activation of both the sympathetic nervous system and HPA axis. These alterations can compromise pancreatic β -cell function, diminish peripheral insulin sensitivity, and enhance hepatic gluconeogenesis, collectively contributing to glucose dysregulation. Another experiment showed that delaying sleep by two hours resulted in reduced neuronal activity, decreased glucose uptake into the arcuate nucleus (mediated by the SCN), and the development of hyperglycemia. In addition, studies demonstrate melatonin's

glycemic influence via insulin secretion regulation and insulin sensitivity improvement. In nocturnal rodents, melatonin acts on pancreatic melatonin receptors to regulate insulin and glucagon secretion in a diurnal manner [8]. However, since these findings are based on research in nocturnal serrated animals, their applicability to humans remains unclear, and the role of melatonin in human glucose regulation requires further investigation.

Restless Leg Syndrome (RLS) is clinically characterized by an irresistible urge to move the limbs, typically accompanied by uncomfortable sensations. The disorder's pathophysiology involves impaired function of dopaminergic neurons in the substantia nigra, which are crucial for motor regulation. Iron deficiency has been implicated in this neuronal dysfunction, contributing to RLS development. Recent studies have demonstrated a significantly higher prevalence of RLS among diabetes patients compared to the general population, with approximately 25% (1 in 4) of diabetes patients suffering from RLS. Other clinical studies report an incidence rate of 13.3% in this patient population [9]. While numerous investigations have established the association between type 2 diabetes and RLS, the relationship cannot be entirely attributed to peripheral neuropathy alone. RLS patients frequently experience leg discomfort at night, which may exacerbate pre-existing neuropathic symptoms. Diabetes neuropathy itself can also induce nerve damage, leading to abnormal sensory perceptions that worsen RLS manifestations, thereby creating a vicious cycle. Furthermore, RLS patients often exhibit concurrent neuroinflammation and oxidative stress, both of which also increase the risk of nerve damage. Beyond its neurological implications, RLS significantly impacts metabolic regulation. Affected individuals commonly suffer from sleep disturbances, including difficulty initiating sleep and frequent nocturnal awakenings due to leg discomfort. These sleep disruptions lead to chronic sleep deprivation, which impairs insulin sensitivity and compromises glycemic control, ultimately exacerbating diabetes management challenges.

3. Treatment strategies for sleep disorders in diabetes

Current therapeutic approaches for disease management encompass multiple modalities: (1) continuous positive airway pressure (CPAP) therapy, (2) pharmacological interventions, (3) lifestyle and behavioral modifications, and (4) chronotherapeutic strategies targeting circadian regulation. Continuous positive airway pressure (CPAP) therapy is the standard treatment for OSA. CPAP therapy is the gold standard for treating OSA [10, 11]. However, despite the proven effectiveness of CPAP in reducing OSA symptoms and related health risks and diseases, the usage rate of CPAP among patients is still very low, with reported non-use rates ranging from 29% to 83% [12]. Continuous positive airway pressure ventilation provides a constant, fixed airway pressure to prevent respiratory collapse during sleep, which makes it the most effective treatment for most patients after diagnosis. Its working principle is mainly to provide two distinct pressure levels- higher during inhalation and lower during exhalation. This treatment improves nighttime hypoxia, reduces insulin resistance, enhances cellular insulin sensitivity, and stabilizes blood sugar fluctuations [8]. However, research on pharmacological treatments for sleep disorders in type 2 diabetes patients remains limited. Related available research results show that one third of type 2 diabetes patients use hypnotics. The most commonly prescribed pharmacological treatments include hydroxyzine, benzodiazepines, and non-benzodiazepine hypnotics (zolpidem, zaleplon), whereas melatonin and herbal remedies are typically utilized as alternative or adjunctive therapies [13]. Evidence suggests that the use of benzodiazepines and zolpidem significantly increased the risk of developing type 2 diabetes [14]. In addition, long-term use of hypnotics, particularly benzodiazepines, has been associated with several adverse effects, including worsening memory impairment, increased fall risk, and reduced life expectancy [14-16].

At the same time, the improvement of lifestyle can significantly alleviate the insomnia symptoms in diabetes patients. Fluctuations in blood sugar, nocturnal polyuria, neuropathy, etc. may affect sleep,

while poor long-term sleep quality will aggravate insulin resistance and uncontrolled blood sugar. The following lifestyle changes can positively impact sleep: regular sleep patterns, establishing a healthy circadian rhythm, reducing bedtime stimulation, avoiding the use of devices such as computers and phones, optimizing the sleeping environment, and maintaining a quiet and dark bedroom. Moderate exercise, avoid vigorous exercise, and choose aerobic exercise that suits oneself. Regarding diet, avoid excessive use of caffeine and alcohol near bedtime, and avoid interfering with sleep and sleep structure [8].

4. Conclusion

In general, insufficient sleep can affect blood sugar stability in various ways, including hormonal imbalances (such as changes in growth hormone and melatonin levels), increased inflammation and oxidative stress, and neurological dysfunction. It will also cause complications in diabetes patients, which will damage multiple organs. Addressing this issue needs to be further studied, explored, and the continuous development of new treatment strategies. Good blood sugar control can help prevent the occurrence of these diseases, improve quality of life, prolong lifespan, reduce hospitalization rates, enhance daily living abilities, and improve life independence. Diabetes brings huge medical expenses. Effective management of blood sugar not only reduces the personal expenses of patients but also reduces the expenses of the medical insurance system. Diabetes is a chronic metabolic disease characterized by hyperglycemia. More and more studies indicate that sleep disorders are highly present in diabetes patients, which seriously affects the quality of life of patients. However, the traditional management of diabetes often ignores the systematic evaluation and intervention of sleep problems, so more and more optimized methods are needed to comprehensively treat the sleep disorders of diabetes patients.

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