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Quality of Sleep and Its Effect on Glycemic Control

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Abstract

Diabetes mellitus (DM) is a widespread illness that affects around 347 million individuals globally. DM not only has many clinical implications but also has a detrimental impact on the quality of sleep in patients. Insufficient sleep quality hinders the proper regulation of blood sugar levels, which is considered a fundamental aspect of managing diabetes. It also has other harmful repercussions that significantly affect one's overall quality of life. Increasing data suggests that sleep disturbances and sleep deprivation have an impact on glucose metabolism and insulin resistance. Simultaneously, changes in glucose metabolism can potentially affect the quality of sleep. The association between T2DM and sleep-disturbed breathing has been thoroughly investigated. Individuals diagnosed with T2DM exhibit a remarkably elevated incidence of obstructive sleep apnea, which subsequently leads to suboptimal management of blood sugar levels. Conversely, the correlation between T1DM and sleep has not been well-studied.

Keywords: Sleep, Glycemic, DM, T1DM, T2DM, Sleep quality.

Introduction:

Diabetes mellitus (DM) is a collection of metabolic illnesses characterized by elevated levels of glucose in the blood, known as hyperglycemia. Type 1 Diabetes Mellitus (T1DM) is distinguished by a complete lack of insulin caused by the immune system destroying the insulin-producing cells. On the other hand, Type 2 Diabetes Mellitus (T2DM) is characterized by the body's resistance to insulin, diminished ability to produce insulin, insensitivity of tissues to insulin, and excessive production of glucose by the liver [1,2]. Diabetes mellitus is a prevalent global health issue that causes substantial illness and death.

According to the American Diabetes Association (ADA) guidelines of medical care in diabetes, poor glycemic control is characterized by an average fasting blood glucose (FBG) level of 152 mg/dl in three measurements, which is equivalent to a HbA1C level of 7%. Despite the administration of medication, patients fail to achieve glycemic control at the target level. This is associated with the emergence of both macro- and microvascular problems, either through direct or indirect means. These complications are frequently observed in individuals with T2DM, such as limb amputations, peripheral neuropathy, advanced kidney disease (nephropathy), heart disease, stroke, and eye disease [3].

The frequency of inadequate glycemic control in patients with T2DM is rising and is reported with variability across the globe. This statistic was derived from a study conducted in Malaysia, where 72% of the participants were found to have this outcome. Additional studies have demonstrated that individuals in the United States experience a 76% impact from inadequate glycemic management. Similarly, Venezuela and Hawaii report a 76% and 68.5% effect, respectively. Jordan and Kenya also exhibit significant effects with rates of 65.1% and 60.5%, respectively [4].

Enhancing the duration and quality of sleep to enhance glycemic management in people with type 2 diabetes mellitus. Given the connection between sleep and hormonal changes that affect how the body processes glucose, it is essential to examine how sleep length and quality are related to glycemic management. The management of blood sugar levels is the most formidable issue confronting the Ethiopian population with T2DM. Nevertheless, there has been a lack of study regarding the relationship between sleep length and sleep quality in individuals with diabetes mellitus [5].

A comprehensive literature search was conducted in nine electronic databases from the beginning until August 2015, without any limitations on language, to evaluate the influence of sleep duration and sleep quality on the regulation of blood sugar levels in individuals with type 2 diabetes. The search yielded 20 papers, with eight focusing on sleep duration and 15 examining sleep quality. The findings of this study indicate that both the quantity and quality of sleep play a significant role in the metabolic function of individuals with type 2 diabetes [6].

A cross-sectional study was conducted at Felege Hiwot Comprehensive Referral and Specialized Hospital in Northwest Ethiopia to evaluate the relationship between glycemic control and sleep quality, sleep duration, and napping in patients with type 2 diabetes mellitus. The study revealed a high prevalence of poor glycemic control among these patients. There was a statistical association between poor glycemic control and factors such as poor sleep quality, both insufficient and excessive sleep length, and a moderate or low likelihood of obstructive sleep apnea. Therefore, it is advisable to prioritize both the quality and duration of sleep in order to effectively regulate glycemic management within the optimal range [4].

A study was conducted to assess the impact of sleep quality and quantity on glycemic control in adults with type 1 diabetes. The findings revealed that inadequate sleep quality is linked to reduced time spent within the desired glycemic range and increased variability in blood sugar levels. Therefore, enhancing sleep quality in individuals with type 1 diabetes may lead to improved glycemic control [7].

Understanding Glycemic Control:

Effective glycemic control is essential for the management of diabetes. A1C values beyond 7.0% are linked to a considerably higher risk of both microvascular and cardiovascular problems, regardless of the specific medication being used. The initial data from the Diabetes Control and Complications Trial (DCCT; type 1 diabetes) and the United Kingdom Prospective Diabetes Study (UKPDS; type 2 diabetes) revealed a curved relationship between A1C levels and the occurrence of diabetes complications. There was no clear threshold at which the benefits of reducing A1C levels stopped. However, it is important to note that the risk reduction was significantly lower at lower A1C levels. Both fasting plasma glucose and postprandial plasma glucose (PPG) are directly linked to the risk of problems. There is some evidence suggesting that PPG may be a more significant independent risk factor for cardiovascular (CV) issues [8-10].

Research suggests that achieving better control over blood sugar levels decreases the likelihood of experiencing both small blood vessel-related issues and cardiovascular complications. The early trials were undertaken in individuals who had been recently diagnosed with diabetes, using a prospective randomized controlled design. The DCCT study in type 1 diabetes, the Kumamoto trial, and the UKPDS trial in type 2 diabetes all demonstrated that better management of blood sugar levels dramatically decreased the likelihood of developing small blood vessel-related problems. However, there was no notable impact on cardiovascular outcomes. Further observational data collected during the extended monitoring period following the end of the randomized phases of both the DCCT and UKPDS studies revealed a continued presence of significant improvements in microvascular health [11,12].
Additionally, it was observed that intensive glycemic control had a positive impact on cardiovascular outcomes. This phenomenon has been referred to as "metabolic memory" or "legacy effect". Within the DCCT cohort, participants who had received intensive treatment previously experienced a noteworthy decrease in cardiovascular (CV) events by 42%, nonfatal myocardial infarction (MI), stroke, and CV-related death by 57%, as well as a reduction in all-cause mortality by 33% compared to those who had previously received conventional treatment. Similarly, the UKPDS cohort observed a noteworthy decrease in the occurrence of myocardial infarction (MI) ranging from 15% to 33%, as well as a decline in overall mortality rates ranging from 13% to 27%. These improvements were observed specifically in people who were initially assigned to receive intensive therapy [13,14].

The Importance of Quality Sleep:

Undoubtedly, sleep is an essential physiological process crucial for human survival. Nevertheless, as economic and societal pressures continue to rise, the significance of chronic sleep deprivation has been recognized [15].
The amount of sleep falls from approximately 18 to 16 hours per day in newborn infants to 7 to 6 hours in older persons. These age-related alterations are widely recognized. While the reasons for these changes and the elements that influence them remain unknown, several recommendations have been made regarding the ideal amount of sleep for different age groups. Age is not the sole factor that determines the amount of sleep one gets. There is a significant variation in the amount of sleep across different countries. An Internet survey was conducted to evaluate sleep duration among children aged from birth to 36 months in 17 countries/regions, which were mostly Asian and predominantly Caucasian. The study found that the overall amount of sleep varied between 11.6 hours in Japan and 13.3 hours in New Zealand. The variations observed in sleep duration may be attributed to cultural disparities [16].
Objective definition of sleep quality is challenging. The polysomnographic recording of a person may display a sleep progress chart that exhibits a higher occurrence of deep sleep in the initial third of the night, followed by an increase in the duration of REM sleep and N2 sleep stage in the final third of the night, along with a low frequency of intermittent waking. However, if the individual is dissatisfied with their sleep during the night, it is considered to be of poor quality. Hence, it is imperative to subjectively determine the quality of sleep [17].

The Correlation Between Sleep and Diabetes:

The importance of adequate sleep cannot be overstated, particularly in the context of chronic medical conditions such as DM. In addition to causing daytime tiredness, poor sleep quality has wide-ranging consequences that impact other parts of life. The relevant factors include: intensification of seizures, impairments in short-term memory, long-term cognitive consequences, and headache. When these factors are combined with the already deteriorated quality of life in patients with chronic conditions, they might result in many harmful repercussions in an individual's life.
According to clinical studies, up to 33% of patients with DM experienced sleep difficulties, while just 8.2% of individuals without DM had similar issues. According to a research poll done at the University of Pittsburgh, over half of the people diagnosed with type 2 diabetes mellitus are likely to report experiencing poor sleep. Patients diagnosed with type 2 diabetes mellitus (DM) exhibited a higher likelihood of experiencing a low Pittsburgh Sleep Quality Index (PSQI). The PSQI is a validated instrument that assesses the quality and pattern of sleep in older individuals. It distinguishes individuals with poor sleep quality from those with regular sleep patterns by evaluating seven aspects of sleep over a period of one month [18].
The measures of these indices include common characteristics related to insomnia, such as sleep latency and efficiency. The aforementioned study also demonstrated a strong correlation between sleep quality and other

measures of diabetic quality of life. Typically, those with additional long-term health concerns are also more prone to experiencing insomnia. Analyzed in a sample of 3282 persons from a large community, polysomnographic data was examined with self-reported sleep patterns and current health status. In patients with DM, the adjusted odds ratio for sleeplessness was 1.4, as compared to individuals without the disease. After controlling for age, gender, and apnea-hypopnea index, it was found that patients suffering from both diabetes mellitus and insomnia had a worse sleep efficiency compared to those who did not have the disease [19,20].

Research has demonstrated a connection between lack of sleep and interrupted sleep patterns with insulin resistance in those who are obese. Inadequate sleep quality has ramifications for the self-management of diabetes. Adult diabetic patients who reported experiencing substandard sleep quality were administered questionnaires to assess their diabetes management, sleep quality, and daytime drowsiness. The study revealed that patients experiencing sleep disturbances exhibited challenges in managing their diabetes [21].

However, no significant correlation was observed between diabetes control difficulties and demographic variables such as education, age, and gender. Research has established a correlation between insufficient sleep and insomnia and a reduction in gamma-aminobutyric acid (GABA). Patients with depression exhibit a decreased amount of GABA. The pancreas produces GABA in substantial quantities. Additionally, it has been demonstrated to hinder the process of programmed cell death in the beta cells of rodents. The enzyme glutamate decarboxylase (GAD), which is primarily responsible for the synthesis of gamma-aminobutyric acid (GABA), has been associated with type 1 diabetes mellitus (DM). GABA may be a neurotransmitter implicated in the sleep quality of diabetics, particularly when its levels are low. Orexins have also been linked to sleep, arousal, energy balance, and feeding. Orexins have been associated with glucose metabolism. Obesity, obstructive sleep apnea, and depression all hinder the expression of this. The causal connection between sleep deprivation and DM has been further clarified in a recent crossover research with fourteen individuals in good health who had a 4-hour reduction in sleep. The limited sleep duration over a certain period resulted in a loss in the body's ability to respond to insulin in the peripheral tissues [22,23].

However, it is worth noting that the sensitivity of the liver to insulin did not decline. There was no notable decrease in slow wave sleep linked to it. There was a little elevation in cortisol and catecholamines. This enhances the process of lipolysis. The levels of non-esterified fatty acids and β-OH butyrate were increased, suggesting an elevation in the breakdown of fats and the oxidation of fatty acids in the liver. The resting energy expenditure remained constant, while the respiratory quotient decreased, indicating a steady increase in fat oxidation. The increased levels of non-esterified fatty acids may alter the functioning of the liver's metabolism. Hence, the insulin resistance is caused by tissues outside the liver [24].

Nocturnal Hypoglycemia:

Sleep disturbance can result from nocturnal hypoglycemia and is considered a contributing factor to the diminished sleep quality experienced by those with diabetes. Extended gaps in self-monitoring glycemia typically occur throughout the nighttime, and this timeframe is linked to the greatest insulin sensitivity. Research examining continuous glucose monitoring has demonstrated that individuals with type 1 diabetes spend an average of 2.3 hours per day with glucose levels below 70 mg/dL, with the majority of these instances occurring during the night. These findings were confirmed by another study employing the same methods of continuous monitoring, which demonstrated that nocturnal hypoglycemia occurred in over half of the nights examined. In addition, different insulin regimens can also increase the likelihood of nighttime hypoglycemia in a patient with diabetes. A comparative research between bedtime insulin NPH (neutral protamine hagedorn) and bedtime insulin glargine revealed a statistically significant difference in the occurrence of nocturnal hypoglycemia, with bedtime insulin NPH having an incidence rate of 24% compared to 9.9% for bedtime insulin glargine [25-27].

Restless Legs Syndrome:

Restless legs syndrome is a sleep problem that is related to the sensorimotor system. It can be classified as either primary or secondary, depending on whether it is associated with other illnesses including anemia, pregnancy, or end-stage renal disease, among others. The International Restless Syndrome Study Group (IRLSSG) has established four crucial criteria for diagnosing patients with restless leg syndrome. It comprises: The individual experiences a strong desire to move their legs, which is accompanied by an unpleasant sensation such as creeping, crawling, pain, itching, or jittering. This sensation is relieved when the person moves their legs and worsens when they are at rest, particularly when trying to fall asleep. Symptoms

tend to worsen in the evening or at night. The upper extremities may also be affected. Women experience Restless Leg Syndrome (RLS) at a rate that is twice as high as men, regardless of the population or age group. There is data that suggests a connection between diabetes mellitus and a higher likelihood of developing Restless Legs Syndrome (RLS). Multiple individuals with diabetes who have restless leg syndrome (RLS) also experience peripheral neuropathy. diabetes individuals with Restless Leg Syndrome (RLS) are more prone to reporting lower sleep quality, experiencing longer time to fall asleep, having decreased sleep efficiency, and encountering more daytime impairment as compared to diabetes individuals without RLS [28-30].

RLS can be managed through non-pharmacological interventions, such as adopting a consistent exercise routine, avoiding all caffeinated foods and beverages, utilizing pneumatic compression devices on the thigh and leg during sleep, receiving massage therapy, and soaking the legs in warm water. Treatment with pharmacotherapy might involve the use of dopamine agonists like pramipexole and ropinirole, anticonvulsants like gabapentin, opiates, benzodiazepines, as well as mineral and vitamin supplementation. Specifically, oral iron supplementation is recommended for individuals with low serum ferritin levels below 50 μg/L. Various pharmaceutical drugs have been linked to exacerbating symptoms of RLS. Common drugs related with RLS include selective serotonin receptor inhibitors, antihistamines, dopamine agonists, and sympathomimetic medications. The substances encompass antihistamines, dopamine antagonists, sympathomimetic drugs, caffeine, nicotine, and alcohol. Efforts should be taken to avoid drugs that can exacerbate RLS and thus compromise the sleep quality of affected people [31,32].

Sleep Disordered Breathing:

Obstructive sleep apnea (OSA) is an intricate condition marked by recurring instances of blockage in the throat during sleep, resulting in repeated episodes of intermittent oxygen deprivation, interruptions in sleep, which in turn can cause sleep disruption, reduced overall sleep duration, and excessive daytime sleepiness. Obesity increases the likelihood of developing both obstructive sleep apnea and insulin resistance. Foster et al. discovered that within a sample consisting of individuals with obesity and type 2 diabetes mellitus, OSA was quite common. In fact, only 13.4% of patients did not exhibit any level of OSA based on a sleep test conducted using a portable monitoring device at home. Within the population of obese adults with type 2 diabetes, 50% of the patients exhibited moderate or severe OSA, as indicated by an apnea-hypopnea index over 15 episodes per hour [33,34].

Researchers are currently studying the connections between obstructive sleep apnea and insulin resistance as well as glucose intolerance mellitus. There is a hypothesis suggesting that persistent intermittent hypoxia, which occurs during bouts of obstructive apneas and hypopneas, may have a causative effect on the development of insulin resistance in patients. Possible mechanisms involved include elevated levels of cytokines in individuals with OSA (plasma IL-6 and TNF-α), heightened sympathetic neural activity, and the secretion of gluco-regulatory neuroendocrine hormones like cortisol. In a study using obese mice, prolonged intermittent hypoxemia worsened fasting hyperglycemia, glucose intolerance, and insulin resistance. A recent study conducted on individuals with uncontrolled diabetes mellitus (HbA1C $\geq$ 7%) found that a significant number of these patients (37.2%) have intermittent hypoxia, a condition resulting from sleep apnea. Moreover, it exhibited a high correlation with inadequate glycemic control. Nevertheless, it remains uncertain if OSA can potentially contribute to the onset of DM in the long run, and further research is necessary to assess this potential cause-and-effect association [34,35].

Conclusion:

In conclusion, DM is a prevalent global disease. DM not only directly disrupts sleep due to symptoms like frequent urination at night, excessive urination, diabetic neuropathy, and neuropathic pain, but it is also linked to various chronic conditions such as obstructive sleep apnea, cardiovascular complications, cerebrovascular accidents, and depression. These conditions can further worsen sleep quality and overall well-being. During their visit to healthcare providers, the patient may not prioritize discussing their sleep concerns, as urgent issues are given priority. Health care professionals must prioritize addressing sleep disorders and the reduced quality of life caused by insufficient and disrupted sleep in patients with DM. This is crucial as it can significantly impact their recovery, diabetes management, and overall well-being. Sleep education should be regarded as a crucial component of the arsenal for managing diabetes.

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