

Sleep Disorders as a Risk Factor for Diabetes or Complications: A Literature Review

Adilla Fida Sauqin¹, Atika^{2*}

¹Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

²Department of Public Health Science-preventive Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

E-mail: adilla.fida.sauqina-2021@fk.unair.ac.id; atika@fk.unair.ac.id

*corresponding author details: Atika; atika@fk.unair.ac.id

ABSTRACT

Sleep disorders are a common health problem that can affect various aspects of the body's metabolism, including the risk of diabetes mellitus (DM) and its complications. Research shows that poor sleep quality or inadequate sleep duration can increase the risk of developing type 2 DM as well as worsen the condition of patients who have already been diagnosed. The mechanisms involved include impaired glucose regulation, insulin resistance and systemic inflammation. In addition, sleep disorders such as obstructive sleep apnea (OSA), insomnia, and restless legs syndrome also contribute to the development of chronic complications of DM, such as cardiovascular disease and diabetic neuropathy. This literature review aims to identify the relationship between sleep disorders and the risk of diabetes or its complications based on current scientific evidence. The analysis showed a significant association between poor sleep quality and increased risk of DM and long-term complications. Understanding this association allows for more effective prevention and intervention measures, such as raising awareness of the importance of sleep management in high-risk populations. Further research is needed to strengthen these findings and explore more in-depth mechanisms so that optimal prevention and treatment strategies can be developed. Sleep health awareness should be an integral part of diabetes management to improve patients' quality of life.

Keywords: sleep disorders; diabetes mellitus; diabetes complications; sleep.

INTRODUCTION

Sleep disorders, such as insomnia, sleep apnea, and suboptimal sleep duration, have been identified as contributing factors to increased risk of type 2 diabetes mellitus and other metabolic complications. Diabetes mellitus itself is a chronic disease that is often found worldwide, with increasing prevalence, especially in developing countries [1]. The relationship between sleep disorders and diabetes is reciprocal: sleep disorders can interfere with blood glucose control and increase the risk of insulin resistance, while diabetes can also affect sleep quality due to conditions such as neuropathic pain, increased urinary frequency at night, or hypoglycemia during sleep[2].

Epidemiological studies have shown that sleep duration that is too short (<6 hours) or too long (>9 hours) is associated with an increased risk of diabetes [3]. This relationship is influenced by hormonal changes, including increased cortisol levels and imbalances in hormones that regulate appetite, such as ghrelin and leptin [4]. This imbalance contributes to weight gain and obesity, which is a major risk factor for type 2 diabetes.

Obstructive sleep apnea (OSA) is common in individuals with diabetes and can worsen blood glucose control [5]. This occurs through mechanisms such as chronic intermittent hypoxia and increased sympathetic nervous system activity [6]. Therapy for sleep disorders, including the use of Continuous Positive Airway Pressure (CPAP), has been shown to effectively improve sleep quality and assist in glucose management in patients with this condition [7].

Obstructive sleep apnea is common in individuals with diabetes and may impair blood glucose regulation through mechanisms such as chronic intermittent hypoxia and increased sympathetic nervous system activity [8]. The use of sleep therapy, such as Continuous Positive Airway Pressure (CPAP), has been shown to be effective in improving sleep quality while assisting with glucose management in patients with this condition [7].

Management of sleep disorders is an important part of holistic diabetes management efforts, given its significant impact on patients' metabolism and quality of life.

REVIEW CONTENT

Type 2 Diabetes Mellitus

Definition of type 2 diabetes mellitus

Diabetes mellitus is a widespread disease in Indonesia and a serious concern at the global level. This spread is influenced by various factors related to rapid cultural and social changes. Urbanization, for example, has changed the lifestyle of many individuals, including unhealthy eating habits. In addition, the increase in the elderly population, sedentary habits, and unhealthy lifestyles have exacerbated the situation. These conditions can reduce the quality of life of diabetes mellitus patients, as well as reduce life expectancy due to complications that may arise [9].

Prevalence of type 2 diabetes mellitus

WHO (World Health Organization) states that the prevalence of type II diabetes mellitus (T2DM) is increasing worldwide, especially in developing countries. The latest data from the International Diabetes Federation (IDF) (2021) reports that type II diabetes mellitus affects 537 million people worldwide. Diabetes mellitus directly causes about 1.5 million deaths each year. Type 2 diabetes mellitus is the most common type of diabetes in Indonesia, which is around 90-95% of total diabetes patients based on data from the Health Office of the Republic of Indonesia [10].

Pathophysiology of type 2 diabetes mellitus

Type 2 diabetes mellitus is a type of diabetes caused by a disturbance in the function of the hormone insulin, which makes insulin insufficiently effective or insensitive to its receptors. This results in the insulin produced not being utilized properly by the body, a condition known as insulin resistance. Type 2 diabetes is characterized by elevated blood glucose levels (hyperglycemia) accompanied by metabolic disorders, which include disturbances in the processing of carbohydrates, fats, and proteins due to the body's inability to use insulin optimally [11].

Type 2 diabetes mellitus begins with the body trying to maintain normal glucose levels through increased insulin production. However, as the disease progresses, beta cells are damaged, and the insulin produced is no longer enough to control glucose levels, leading to hyperglycemia. Most patients with type 2 DM are also obese, with body fat accumulating mainly in the abdominal area. This fatty tissue increases insulin resistance through inflammatory processes, which include excessive free fatty acid (FFA) release and adipokine imbalance.

Type 2 diabetes mellitus screening criteria

Hyperglycemia in type 2 diabetes mellitus is characterized by elevated blood glucose levels. Normal fasting blood glucose levels according to WHO are between 70 mg/dL (3.9 mmol/L) and 100 mg/dL (5.6 mmol/L). Elevated fasting blood glucose levels are an indicator of higher risk of diabetes. The criteria for diagnosis of type 2 DM can refer to the guidelines issued by the Ministry of Health in 2022.

- (1) Fasting blood sugar (GDP), an examination conducted after fasting for approximately 8 hours using a blood sample from the patient's vein. Patients can be said to have type II DM if the test results show fasting blood sugar levels greater than, or equal to, 126 mg/dL.
- (2) Oral glucose tolerance test (OGTT), is an examination conducted after 2 hours of glucose administration of about 75 grams by taking venous blood samples. Patients are diagnosed with type II DM if the test results show more than or equal to 200 mg/dL blood glucose level.
- (3) Whole blood sugar (GDS) is a test that is done using a venous blood sample and can be done at any time, without preparation. A person can be diagnosed with type II DM using this test if the result is greater than or equal to 200 mg/dL.
- (4) Hemoglobin A1c (HbA1c) is a test performed with a method standardized by the National Glycohemoglobin Standardization Program (NGSP) using the patient's venous blood sample. Patients can be diagnosed with type II DM if the HbA1c level is greater than or equal to 6.5%.

Hyperglycemia is not the only risk factor for diagnosing diabetes mellitus. In fact, there are other factors of diabetic patients that trigger the occurrence of type II diabetes mellitus.

Factors causing type 2 diabetes mellitus

In general, the clinical symptoms that occur in type II diabetes mellitus are difficult to identify, but there are several things that characterize patients with type II diabetes mellitus based on data from WHO, CDC and PERKENI 2021 including

- (1) Age
prevalence of diabetes increases with age [12] Almost half of all type II diabetes mellitus patients are adults aged ≥ 65 years [13]. Older adults with T2DM have limitations that make it difficult to maintain good health for example, increased susceptibility to hypoglycemia, increased dependence on care, the potential presence of multiple comorbidities and the effects of frailty all add to the complexity of managing diabetes mellitus in this age group [13].
- (2) Gender
The prevalence of type 2 diabetes mellitus increases in both sexes, but men are usually diagnosed at a younger age and lower body fat mass than women. Postprandial hyperglycemia increases to a greater extent in women with age, contributing to the higher prevalence of undiagnosed diabetes in women after age 60 [14].
- (3) Race and ethnicity
In a systematic review of the literature there were significant differences in blood sugar control by race/ethnicity [15]. African American, Hispanic and Asian populations were found to have significantly higher HbA1c levels compared to non-Hispanic whites.

(4) Obesity

Based on data from the Ministry of Health [16], a person can be said to be obese if overweight/IMT \geq 25 kg/m² and abdominal circumference if in men $>$ 90 cm and women $>$ 80cm. Obesity is a major, potentially modifiable risk factor for type 2 diabetes mellitus. In obesity, insulin sensitivity, as well as modulation of β -cell function, is decreased. Obesity tends to run in families, and families often have similar eating and exercise habits [17].

(5) Physical activity less than 3 times a week

Lack of physical activity is one of the most common risk factors in patients with type 2 diabetes mellitus. This occurs because the presence of free fatty acids released from adipose tissue causes a decrease in insulin sensitivity in muscle, fat and liver tissue, and is followed by an increase in blood glucose levels, and insulin resistance and type 2 diabetes mellitus can occur. Lack of physical activity can accelerate the pathogenesis of type 2 diabetes mellitus, leading to morbidity and mortality [18].

(6) Nutrition (carbohydrate, fat intake, fiber)

Several studies have found a strong association between T2DM and high carbohydrate and fat intake. Many studies have reported a positive association between high sugar intake and the development of T2DM [19].

(7) Family history of diabetes mellitus

The American Diabetes Association states that T2DM is more strongly linked to family history and ancestry than type 1, and studies of twins show that genetics play a particularly strong role in the development of T2DM.

(8) Hypertension/High blood pressure ($>$ 140/90 mmHg)

After reaching the intermediate stage of diabetes, vascular remodeling has developed and peripheral vascular resistance also contributes to hypertension. In addition, vascular remodeling greatly influences diabetic complications (Ohishi 2018).

Physical symptoms of type 2 diabetes mellitus

In general, the clinical symptoms that occur in type II diabetes mellitus are difficult to identify, but there are several things that characterize patients with type II diabetes mellitus based on data from WHO, CDC and PERKENI 2021 including.

- (1) Frequent urination at night (polyuria)
- (2) Feeling Extremely Thirsty (polydipsia)
- (3) Easy hunger (Polyphagia)
- (4) Unintentional weight loss
- (5) Have blurred or unclear vision
- (6) Feeling very tired
- (7) hard-to-heal wounds
- (8) Frequent tingling sensation in hand and feet
- (9) acanthosis nigricans

Sleep**Sleep physiology**

Sleep is one of the unconscious states of a person that can be awakened by sensory stimulus or the presence of other awakening factors [20].

There are two general processes that are considered significant in sleep physiology: circadian rhythm and homeostasis. Circadian rhythms are day-night cycles within a 24-hour period that consist of patterns of wakefulness and drowsiness [21]. These circadian rhythms are influenced by the suprachiasmatic nucleus (SCN) of the hypothalamus [22]. Sleep patterns will follow the circadian rhythm system governed by the suprachiasmatic nucleus (SCN) of the hypothalamus. GABAergic sleep triggers are found in the brainstem, lateral hypothalamus, and preoptic area [23].

Sleep Stages

There are two fundamentally different types of sleep: rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep [24].

- NREM (non-rapid eye movement)

There are 4 stages in NREM. Stage 1 includes the onset of sleep and is characterized as light sleep, stage 2 is the stage where muscles begin to shut down. Stages 3 and 4 are also known as SWS (slow-wave sleep), which is deep sleep with prominent slow brain waves and is associated with minimal mental activity. NREM sleep typically accounts for 75-80% of TST (total sleep time ratio). In the NREM sleep stage, it can be said to be a restorative and healing time for the body [21].

NREM is often referred to as dreamless sleep, but basically this stage also has dreams and sometimes nightmares can occur during the NREM sleep stage. The difference with dreams that exist in the REM stage is that dreams that occur in the REM stage often involve contractions of the body's muscles while in the NREM stage dreams that occur are more often rarely remembered by us. It can be concluded that dreams at the stage of slow wave sleep (NREM) are not linked into memory [20].

(1) N1 (Stage 1) - Light Sleep (5%)

This stage lasts about 1 to 5 minutes, comprising 5% of the total sleep time (Patel, et al, 2018). This stage is also a transitional stage between waking and sleeping. The characteristics of this stage are, there is still a sense of drowsiness, movement of the eyeballs, awareness of the surroundings, decreased pulse and respiratory rate (Rosyaria & Khairoh, 2019).

(3) N2 (Stage 2) - Deeper Sleep (45%)

This stage represents deeper sleep when the heart rate and body temperature decrease (Patel, et al, 2018). This stage is also a light sleep stage, lasting about 10-15 minutes, but makes up about 40%-45% of total sleep. The characteristics of this stage include decreased heart rate and breathing frequency, decreased body metabolic processes, decreased body temperature, and almost the same eye position as stage I (Rosyaria & Khairoh, 2019).

N3 (Stage 3 and 4) - Deepest Non-REM Sleep (25%)

This stage is also known as slow wave sleep (SWS).

This stage of sleep is characterized by a much lower frequency signal and a fairly high amplitude or more commonly known as delta waves. This stage is the most difficult to wake up, and for some people, even loud noises (>100 decibels) will not wake them up (Patel, et al, 2018). At this stage of sleep all physiological processes will decrease due to the parasympathetic nerves that work more dominantly so that someone is more difficult to wake up at this stage (Rosyaria & Khairoh, 2019).

- REM (Rapid eye movement)

In the REM stage, it is often associated with dreams. This stage accounts for about 20-25% of total sleep time. The activity that occurs in the brain during the REM stage is said to be similar to wakefulness. This REM stage describes the brain in a very active state with a paralyzed body [24]. In this stage there are irregular muscle movements despite very strong resistance in the peripheral muscles. This state particularly includes rapid eye movements. In REM sleep, metabolism throughout the brain increases by 20% compared to the NREM stage [20].

Sleep quality

Sleep quality according is a person's satisfaction with sleep, so that a person does not show feelings of fatigue, easily aroused and restless, lethargy and apathy, blackness around the eyes, swollen eyelids, red conjunctiva, sore eyes, fragmented attention, headaches and frequent yawning or drowsiness [25]. Sleep quality consists of quantitative aspects, such as total sleep time, sleep latency, frequency of awakening, as well as subjective and qualitative aspects. People who experience sleep problems also tend to have poor sleep quality, which may be an important symptom of medical problems, therefore more attention should be paid to the patient's sleep quality [26].

Sleep quality can be defined as the satisfaction felt with sleep. This satisfaction can be evaluated subjectively by the individual's feelings about their sleep and objectively by the amount of sleep obtained. [27] indicate that sleep quality is an individual's assessment of the degree to which sleep-related characteristics satisfy individual needs. Sleep characteristics consist of sleep quality, amount of sleep, and factors that are indirectly related to sleep, such as the use of sleeping pills. Sleep quality takes into account subjective feelings of overall sleep quality, sleep disturbance, and sleep satisfaction. Sleep amount includes actual hours of sleep, sleep latency, and sleep efficiency.

Components of sleep quality

The components of sleep quality that can be studied [27][28]. namely:

- (1) Subjective sleep quality

Subjective self-assessment of the quality of sleep you have. The existence of feelings of disturbance and discomfort in oneself during sleep which can affect sleep quality [28].

- (2) Sleep duration

Judged from the time of starting sleep to the time of awakening, unfulfilled sleep time will cause poor sleep quality [28].

- (3) Sleep latency

The amount of time it takes for a person to fall asleep, this relates to a person's sleep waves [28].

- (4) Sleep efficiency

Sleep efficiency is obtained through the percentage of human sleep needs, by assessing a person's sleep hours and sleep duration, sleep duration so that it can be concluded whether it is sufficient or not [28].

- (5) Sleep disturbances

Snoring, frequent movement disorders and nightmares can affect a person's sleep process. Sleep states that change from the usual pattern are called sleep disorders. Sleep disturbance problems are common in adults with sleep disorders and are associated with increased sympathetic nervous system activity and the hypothalamic-pituitary-adrenal axis, the effects of metabolic changes, circadian rhythms, and proinflammatory responses [28].

- (6) Sleep medication use

Sleeping pills can indicate how severe the sleep disorder is, because the use of sleeping pills is indicated if the person has a very disturbed sleep pattern and sleeping pills are considered necessary to help sleep [28].

- (7) Daily activity dysfunction

A person will feel awake feeling unrefreshed, frequent drowsiness during the day, difficulty concentrating, and easily tired as a result of poor sleep quality not [28].

Sleep quality in patients with type 2 diabetes mellitus

Research reports that approximately 32.2% of patients with type 2 diabetes mellitus (T2DM) experience sleep disturbances [29]. Studies comparing T2DM patients with healthy individuals show that higher glycated hemoglobin (HbA1C) levels are associated with lower sleep efficiency, increased sleep movement time, and impaired glucose metabolism. These factors contribute to decreased sleep quality in T2DM patients [30].

Sleep quality in patients with diabetes mellitus is influenced by various factors, including physical, psychosocial, and environmental aspects [31]. Psychological issues also play a significant role, with type 2 diabetes patients tending to have a lower sleep quality index (PSQI) [32] [27]. Difficulty initiating and maintaining sleep is often experienced as a result of disorders affecting sleep patterns, ultimately worsening patients' quality of life [33][34].

Lack of sleep at night can lead to drowsiness, fatigue, depression, and reduced activity and health during the day.

Chronically short sleep duration is associated with increased risk of obesity, type 2 diabetes, hypertension, cardiovascular disease, depression, and premature death [35]. Therefore, it is important for medical personnel to pay special attention to sleep problems in diabetic patients during treatment.

CONCLUSIONS

Sleep disorders, such as obstructive sleep apnea, insomnia, and non-ideal sleep duration, have been shown to be significant risk factors for diabetes mellitus (DM) and its complications. Sleep disorders can affect glucose metabolism, increase insulin resistance, and worsen glycemic control in patients with DM. Conversely, people with DM are also more susceptible to sleep disturbances due to clinical conditions such as diabetic neuropathy and night polyuria.

Effective management of sleep disturbances has the potential to improve the quality of life of diabetic patients and prevent long-term complications. Therefore, more attention is needed to the evaluation and intervention of sleep disorders in DM care. Further research is urgently needed to deepen the understanding of the mechanisms of the relationship between sleep disorders and diabetes and to develop more effective intervention strategies.

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