Review Article

Diabetes and daytime sleeping: systematic review

Comment [GG1]: Title ok

Abstract:

Comment [GG2]: Ok

Background: The relationship between sleep disturbance and diabetes is dual-sided. Chronic sleep disturbances would elevate the risk of developing insulin resistance, while diabetes would worsen the quality of sleep.**Objective:** to address the aspects of insufficient sleep, diabetes mellitus, and their mutual interactions and interlinkages. The main objectives isto address the role and effect of diabetes on sleep. Methods: systematic review. A systematic search was done in PubMed, MEDLINE through Clarivate, Web of Science through Clarivate, and EBSCO. Studies retrieved were managed in Rayyan–Intelligent systematic reviews website for duplicate removal and screening. **Result:** DM is one of the most common diseases worldwide. DM, in addition to causing direct sleep disturbances as a result of nocturia, polyuria, diabetic neuropathy and neuropathy pain, has also been associated with several chronic illness as obstructive sleep apnea, cardiovascular complications, hypertension, cerebrovascular accidents and depression which can impair sleep and quality of life. The patient may not bring the sleep issues during their visit to healthcare providers, with acute issues taking precedence during their visit.**Conclusion**: DM causes night sleep disturbances which eventually leads to daytime sleeping. Sleep education should be considered an essential part in the diabetic management armamentarium.

Keywords: Diabetes mellitus, Sleep quality, Quality of life, Sleep disturbance, Nocturnal hypoglycemia.

Introduction:

Comment [GG3]: Ok

Diabetes mellitus is characterized by chronic hyperglycemia arising from dysregulation of carbohydrate, lipid and protein metabolism. (1) Type 2 diabetes mellitus (T2DM) is the most common form of diabetes, accounting for 90% of cases, affecting over 460 million worldwide with projections expecting this number to rise to over 700 million in

just 25 years. The main cause of T2DM is skeletal muscle, liver and adipose tissue insulin resistance eventually giving rise to pancreatic β-cell dysfunction and failure. (2) These impairments result in a chronic hyperglycemic state which, if left untreated, can cause serious complications including macrovascular and microvascular disease. Mirroring this secular rise in T2DM, over the last century, there has been an inverse decline in sleep duration. (3)

Sleep is important for regulating many physiologic functions that relate to metabolism. Because of this, there is substantial evidence to suggest that sleep habits and sleep disorders are related to diabetes risk. (4)

The relationship between sleep disturbance and diabetes is dual-sided. Chronic sleep disturbances would elevate the risk of developing insulin resistance, while diabetes would worsen the quality of sleep. Both the qualitative and quantitative disturbances in sleep significantly increase the risk of developing diabetes. When taking into consideration quantitative aspect, it should be understood that both the short duration and long duration of sleep are associated with higher prevalence of diabetes, with the lowest risk at 7–8 h per day, though the underlying mechanisms and causes in both the conditions may differ. (5)

Sleep disorders are significantly more common in persons with diabetes as compared to those without diabetes. Multiple factors may contribute to insomnia in persons with diabetes including discomfort or pain associated with peripheral neuropathy, restless legs syndrome, periodic limb movements, and rapid changes in blood glucose levels during night leading to hypoglycemic and hyperglycemic episodes, nocturia and associated depression. (6) Individuals with diabetes have a significantly increased risk of developing depression when compared to their nondiabetic counterparts and depression is one of the important factors contributing to poor sleep in this population. Furthermore, diabetes itself has multiple impacts on central nervous system causing alterations involving neurobehavioral and neurotransmitter functioning and autonomic

functions, and can adversely affect endocrine functions, and hence itself cause sleep disturbances. (7)

Aim:this review aims to address the aspects of insufficient sleep, diabetes mellitus, and their mutual interactions and interlinkages. The main objectives isto address the role and effect of diabetes on sleep.

METHODS AND MATERIALS

Comment [GG4]: ok

Type of the study: Systematic review

SAMPLE & STUDY GROUPS

PubMed and EBSCO Information Services were chosen as the search databases for the publications used within the study, as they are high-quality sources. PubMed being one of the largest digital libraries on the internet developed by the National Center for Biotechnology Information (NCBI) which is a part of the United States National Library of Medicine. Topics concerningthe aspects of insufficient sleep, diabetes mellitus, and their mutual interactions and interlinkages. The main objectives isto address the role and effect of diabetes on sleep were used in the making of the article. The founded articles were screened by titles, and reviewing the abstracts.

Inclusion criteria: the articles were selected based on the relevance to the project which should include one of the following topics; 'Diabetes mellitus, Sleep quality, Quality of life, Sleep disturbance, Nocturnal hypoglycemia'.

Exclusion criteria: all other articles which do not have one of these topics as their primary end, or repeated studies, and reviews studies were excluded.

STATISTICAL ANALYSIS

No software will be utilized to analyze the data. The data wasextracted based on specific form that contains (Title of the publication, author's name, objective, summary, results, and outcomes). Double revision of each member's outcomes wasapplied to ensure the validity and minimize the mistakes.

During articles selection, studies were doubled-reviewed, and their results to assure that we enroll the studies related to the objective of our study, and to avoid or minimize errors in the results.

Table1 :Relationship between diabetes and sleep disturbances (daytime sleep)

Comment [GG5]: ok

Auther and publishing year	Study area	methodology	outcome
Safa Barakat et al, 2019 (8)	Amman, Jordan	A cross-sectional study was carried out at the National Center for Diabetes, Endocrinology and Genetics (NCDEG) in Amman, Jordan.A total of 1,211 (540 male and 671 female) patients with T2DM were recruited. Data were collected using the Pittsburgh sleep quality index (PSQI) to assess the sleep quality with a cutoff point of PSQI ≥ 8. Participants' demographic background data were also recorded. Statistical analysis was conducted using SPSS version 22.	Poor sleep quality was reported in 81% of participants. Multivariate logistic regression analysis revealed that poor sleep quality was significantly associated with high HbA1c
AbdulazizDarraj et al,2018 (9)	Jazan, Saudi Arabia.	An analytical cross-sectional study of 307 diabetic patients in Jazan, Saudi Arabia was conducted in 2018. A multistage cluster random sampling was used to select the study participants. Sleep quality was assessed using the	Poor sleep quality among diabetic patients is a prevalent health problem.The prevalence of poor sleep quality was 55.4% (95% CI 49.7-60.8).

		Pittsburgh Sleep Quality Index (PSQI). Data on patient's characteristics were gathered via patients' interviews, and medical data were collected based on the patients' files. Logistic regression analysis was used to identify the predictors of poor sleep quality.	
SeyedMortezaShamshirgaran et al,2017	Iran	This is a cross-sectional study conducted among diabetic patients referring to Ardabil diabetes clinic in Northwest of Iran. Information on sleep quality was collected using Pittsburg Sleep Quality Index (PSQI). A questionnaire was used to collect data on sociodemographic lifestyle factors and psychological distress.	According to the results of the present study, age, duration of disease, psychological distress and high level of cholesterol were independently associated with poor sleep quality.
Samantha B. J. Schipper et al,2021 (11)	Multinational	A literature search was performed in PubMed from inception until January 2021, using MeSH and tiab search terms indicating sleep disorders and type 2 diabetes mellitus.	Sleep disorders are highly prevalent in people with type 2 diabetes, negatively affecting health outcomes.
Amarabalan Rajendran et al,2012 (12)	India	We enrolled 120 patients with type 2 diabetes who attended an endocrinology clinic in a tertiary-care hospital. Quality of sleep was evaluated in all the	We found a high prevalence of sleep dysfunction in patients with type 2 diabetes.The mean global PSQI score was 7.08 (standard deviation, 3.89),

		patients through the Pittsburgh Sleep Quality Index (PSQI). A Global Sleep Quality score ≥5 discriminates between good and poor sleepers.	which suggested poor sleep quality in this population. Sixty-nine percent of patients had a global PSQI score ≥5, indicating that they were "poor sleepers." The global PSQI score positively correlated with the duration of diabetes and was also independent of other variables such as age, gender, body mass index, HbA1c, or medications.
TadegJemere et al,2019 (13)	Ethiopia	Institution based comparative cross-sectional study was conducted at Jimma University Medical Center (JUMC) from April 5 to May 5, 2018.The Hospital serves for a total of 2594 people with type 2 diabetes during the time of data collection.All adult Type 2 DM patients who were enrolled to JUMC and healthy individuals who came to the hospital for routine purpose were the source populations.	The prevalence of poor sleep quality was 55.6% among people with type 2 diabetes mellitus and 32.3% among controls.
Qi-Hui Jin et al,2012 (14)	china	A total of 130 hospitalized elderly type 2 diabetes were included in the study. Questionnaires and other related clinical data were	Elderly type 2 diabetes mellitus are usually poor sleepers. Sixty percent (78/130) were poor sleepers.

		collected within one week after admission. Patients were divided into two groups: poor-sleeper group and good-sleeper group according to Pittsburgh Sleep Quality Index (PSQI).	
Anitra D M Koopman et al,2019 (15)	Multinational	A systematic search of the literature was conducted in MEDLINE (PubMed) and Embase until March 2018 by investigators A.D.M.K. and F.R., assisted by a librarian. Reference lists of included studies were searched manually for additional studies. In short, the search strategy focused on a combination of these terms and their synonyms: (Type 2 diabetes OR NIIDM OR T2DM OR diabetes) AND (Insomnia OR sleep quality OR disturbed sleep).	The prevalence of insomnia (symptoms) is 39% (95% confidence interval, 34–44) in the T2D population and may be associated with deleterious glycemic control.

Result:

DM is one of the most common diseases worldwide. DM, in addition to causing direct sleep disturbances as a result of nocturia, polyuria, diabetic neuropathy and neuropathy pain, has also been associated with several chronic illness as obstructive sleep apnea, cardiovascular complications, hypertension, cerebrovascular accidents and depression which can impair sleep and quality of life. The patient may not bring the sleep issues

during their visit to healthcare providers, with acute issues taking precedence during their visit.

Discussion:

Comment [GG6]: ok

Clinical research has shown that up to one third of patients with DM suffered from concomitant sleep disorders, as compared with 8.2% of controls without DM (16). In another study, more than half of the patients with type 2 DM are likely to report being "poor sleepers", according to a research poll conducted at University of Pittsburgh. The patients with type 2 DM were more likely to have low Pittsburgh Sleep Quality index (PSQI) (17). (PSQI is a validated tool which measures sleep quality and pattern in older adults. It discriminate poor sleepers from normal by assessing seven components of sleep over a one month time interval) (17). Part of the components of these index's metrics are common insomnia variables, such as sleep latency and efficiency. The same study also showed that the sleep quality correlated well with other diabetic quality of life scores (18). In general, patients with other chronic medical conditions are also more likely to experience insomnia.

Studies have linked poor sleep and insomnia to be associated with decrease in gamma-aminobutyric acid (GABA). A lower level of GABA is also seen in the patients with depression (19). GABA is produced in significant levels in pancreas. It has also been shown to be inhibiting apoptosis of the rodent beta cells. The glutamate decarboxylase the primary enzyme (GAD) involved in the synthesis of GABA has been linked with type 1 DM (20). It is possible that GABA is one of the neurotransmitter involved in the sleep quality among diabetics, when in low levels.

A study conducted in Taiwan found that a short sleep duration was associated with a higher prevalence of diabetes (21). Another study among the Taiwanese population found that both short and long sleep durations were independently associated with newly diagnosed diabetes (22). A meta-analysis to assess the dose-response relationship

between sleep duration and risk of type 2 diabetes concluded that the lowest risk for T2DM is among people who get 7–8 h sleep per day, whereas short and long sleep duration are associated with higher risk of T2DM (23).

Subjective sleep disturbances have been reported in more than one-third of people with type 2 diabetes, which may be attributable to fear of poor blood glucose control and diabetic complications (24). However, the relationship between subjective sleep disturbances and blood glucose levels was inconsistent in previous studies. Some studies have reported an inverse association between subjective sleep disturbances and poor glycemic control in people with type 2 diabetes (25), whereas others reported no relationship between subjective sleep disturbances and serum hemoglobin A1c (HbA1c) level as an indicator of glucose status (26). However, studies that report an association with HbA1c level did not fully exclude or adjust for important risk factors associated with poor sleep quality(27). A study by Shankar et al. on perceived insufficient rest included in the Behavioral Risk Factor Surveillance System (BRFSS) of the USA found that perceived insufficient rest/sleep are found to be independently associated with CVDs, diabetes mellitus and obesity (28).

Conclusion and recommendations: DM causes night sleep disturbances which eventually leads to daytime sleeping. It is important for the health care providers treating the patient with DM to address their sleep issues and the impaired quality of life due to inadequate and fragmented sleep, as it may be severely affect their recovery, control of diabetes as well as quality of life. Sleep education should also be considered an essential part in the diabetic management armamentarium.

References:

1. DeFronzo RA, Ferrannini E, Groop L, et al. Type 2 diabetes mellitus. Nat Rev Dis Primers. 2015; 1:15019. doi:10.1038/nrdp.2015.19
2. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*. 2019; **157**:107843. doi:10.1016/j.diabres.2019.107843
3. Defronzo RA. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. Diabetes. 2009; 58: 773- 795. doi:10.2337/db09-9028
4. Shan Z., Ma H., Xie M., Yan P., Guo Y., Bao W., Rong Y., Jackson C.L., Hu F.B., Liu L. Sleep duration and risk of type 2 diabetes: A meta-analysis of prospective studies. *Diabetes Care.* 2015;38:529–537. doi: 10.2337/dc14-2073. [PubMed] [CrossRef] [Google Scholar]
5. Mallon L., Broman J.-E., Hetta J. High incidence of diabetes in men with sleep complaints or short sleep duration: A 12-year follow-up study of a middle-aged population. *Diabetes Care.* 2005;28:2762–2767. doi: 10.2337/diacare.28.11.2762. [PubMed] [CrossRef] [Google Scholar]
6. Gangwisch J.E., Heymsfield S.B., Boden-Albala B., Buijs R.M., Kreier F., Pickering T.G., Rundle A.G., Zammit G.K., Malaspina D. Sleep duration as a risk factor for diabetes incidence in a large U.S. sample. *Sleep.* 2007;30:1667–1673. doi: 10.1093/sleep/30.12.1667. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
7. Resnick HE, Redline S, Shahar E, Gilpin A, Newman A, Walter R, et al. Diabetes and sleep disturbances: Findings from the Sleep Heart Health Study. *Diabetes Care.* 2003;26:702–9. [PubMed] [Google Scholar]
8. Barakat S, Abujbara M, Banimustafa R, Batieha A, Ajlouni K. Sleep Quality in Patients With Type 2 Diabetes Mellitus. J Clin Med Res. 2019 Apr;11(4):261-266. doi: 10.14740/jocmr2947w. Epub 2019 Mar 18. PMID: 30937116; PMCID: PMC6436571.

9. Darraj A, Mahfouz MS, Alsabaani A, Sani M, Alameer A. Assessment of sleep quality and its predictors among patients with diabetes in Jazan, Saudi Arabia. Diabetes MetabSyndrObes. 2018 Sep 25;11:523-531. doi: 10.2147/DMSO.S178674. PMID: 30288072; PMCID: PMC6163002.
10. Shamshirgaran SM, Ataei J, Malek A, Iranparvar-Alamdari M, Aminisani N. Quality of sleep and its determinants among people with type 2 diabetes mellitus in Northwest of Iran. World J Diabetes. 2017 Jul 15;8(7):358-364. doi: 10.4239/wjd.v8.i7.358. PMID: 28751959; PMCID: PMC5507833.
11. Schipper SBJ, Van Veen MM, Elders PJM, van Straten A, Van Der Werf YD, Knutson KL, Rutters F. Sleep disorders in people with type 2 diabetes and associated health outcomes: a review of the literature. Diabetologia. 2021 Nov;64(11):2367-2377. doi: 10.1007/s00125-021-05541-0. Epub 2021 Aug 16. PMID: 34401953; PMCID: PMC8494668.
12. Rajendran A, Parthsarathy S, Tamilselvan B, Seshadri KG, Shuaib M. Prevalence and correlates of disordered sleep in southeast asianindians with type 2 diabetes. Diabetes Metab J. 2012 Feb;36(1):70-6. doi: 10.4093/dmj.2012.36.1.70. Epub 2012 Feb 17. PMID: 22363924; PMCID: PMC3283830.
13. Jemere T, Mossie A, Berhanu H, Yeshaw Y. Poor sleep quality and its predictors among type 2 diabetes mellitus patients attending Jimma University Medical Center, Jimma, Ethiopia. BMC Res Notes. 2019 Aug 6;12(1):488. doi: 10.1186/s13104-019-4531-6. PMID: 31387638; PMCID: PMC6685256.
14. Jin QH, Chen HH, Yu HL, Li TL. [The relationship between sleep quality and glucose level, diabetic complications in elderly type 2 diabetes mellitus]. ZhonghuaNeiKe Za Zhi. 2012 May;51(5):357-61. Chinese. PMID: 22883333.
15. Koopman ADM, Beulens JW, Dijkstra T, Pouwer F, Bremmer MA, van Straten A, Rutters F. Prevalence of Insomnia (Symptoms) in T2D and Association With Metabolic Parameters and Glycemic Control: Meta-Analysis. J Clin Endocrinol

Metab. 2020 Mar 1;105(3):614–43. doi: 10.1210/clinem/dgz065. PMID: 31603475; PMCID: PMC7110921.

16. Sridhar GR, Madhu K. Prevalence of sleep disturbances in diabetes mellitus. Diabetes Res Clin Pract. 1994;**23**:183–186. [PubMed] [Google Scholar]
17. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;**28**:193–213. [PubMed] [Google Scholar]
18. Luyster FS, Dunbar-Jacob J. Sleep quality and quality of life in adults with type 2 diabetes. Diabetes Educ. 2011;**37**:347–355. [PMC free article] [PubMed] [Google Scholar]
19. Budhiraja R, Roth T, Hudgel DW, Budhiraja P, Drake CL. Prevalence and polysomnographic correlates of insomnia comorbid with medical disorders. Sleep. 2011;**34**:859–867. [PMC free article] [PubMed] [Google Scholar]
20. Amihăesei IC, Mungiu OC. Main neuroendocrine features and therapy in primary sleep troubles. Rev Med Chir Soc Med Nat Iasi. 2012;**116**:862–866. [PubMed] [Google Scholar]
21. Tian J, Dang H, Chen Z, Guan A, Jin Y, Atkinson MA, Kaufman DL. γ-Aminobutyric acid regulates both the survival and replication of human β-cells. Diabetes. 2013;**62**:3760–3765. [PMC free article] [PubMed] [Google Scholar]
22. Adeghate E. Orexins: tissue localization, functions, and its relation to insulin secretion and diabetes mellitus. VitamHorm. 2012;**89**:111–133. [PubMed] [Google Scholar]
23. Rao MN, Neylan TC, Grunfeld C, Mulligan K, Schambelan M, Schwarz JM. Subchronic sleep restriction causes tissue-specific insulin resistance. J Clin Endocrinol Metab. 2015;**100**:1664–1671. [PMC free article] [PubMed] [Google Scholar]
24. Shan Z., Ma H., Xie M., Yan P., Guo Y., Bao W., Rong Y., Jackson C.L., Hu F.B., Liu L. Sleep duration and risk of type 2 diabetes: A meta-analysis of prospective

studies. *Diabetes Care.* 2015;38:529–537. doi: 10.2337/dc14-2073. [PubMed] [CrossRef] [Google Scholar]

25. Knutson KL, Ryden AM, Mander BA, Van Cauter E. Role of Sleep Duration and Quality in the Risk and Severity of Type 2 Diabetes Mellitus. *Arch Intern Med.* 2006;**166**(16):1768–74. doi: 10.1001/archinte.166.16.1768. [PubMed] [CrossRef] [Google Scholar]
26. Lecube A, et al. Global assessment of the impact of type 2 diabetes on sleep through specific questionnaires: A case-control study. *PLoS One.* 2016;**11**:e0157579. doi: 10.1371/journal.pone.0157579. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
27. Cho EH, Lee H, Ryu OH, Choi MG, Kim SW. Sleep disturbances and glucoregulation in patients with type 2 diabetes. *J Korean Med Sci.* 2014;**29**(2):243–7. doi: 10.3346/jkms.2014.29.2.243. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
28. Shankar A., Syamala S., Kalidindi S. Insufficient rest or sleep and its relation to cardiovascular disease, diabetes and obesity in a national, multiethnic sample. *PLoS ONE.* 2010;5:e14189. doi: 10.1371/journal.pone.0014189. [PMC free article] [PubMed] [CrossRef] [Google Scholar].