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RESEARCH

Combined Diabetes and Arthritis are Associated with Increased Sleep Efficiency Variability

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Abstract

This research was conducted to observe the effects of diabetes mellitus (DM) and rheumatoid arthritis (RA) on sleep efficiency and to explore the physiological mechanisms contributing to night-to-night sleep variability. Inconsistent sleep schedules or night-to-night sleep variability are arising concerning harmful health consequences. This research used the Midlife in United States Second Wave Research (MIDUS-2). The design was a cross-sectional research consisting of 434 participants. Data was collected from all the participants after taking informed consent. Participants were divided into four groups based on the presence of any systemic disorder. Age, gender, body mass index (BMI), symptoms of depression, and prescribed medicines were included as control variables. Data has been analyzed on SPSS. Of 434 participants, 61.05% were female, 39.63% only had RA, 0.06% had DM alone, and 44.23% were healthy; that is, they were the control group. The sleep efficiency of the healthy group was 81.55%, of patients having only RA was 78.37%, of patients having only DM was 75.35%, and the group having both disorders was 74%. DM is a chronic condition that develops due to a lack of capability to produce energy. RA is a painful autoimmune disorder. The research's results showed a marked difference in the sleep efficiency of these patients.

Keywords Diabetes · Arthritis · Sleep efficiency · Sleep efficiency variability · Diabetes mellitus

Abbreviations

RA	Rheumatoid arthritis
DM	Diabetes mellitus
IL	Interleukin
TNF	Tissue necrotic factor
SLE	Systemic lupus erythematous
BMI	Body mass index

Introduction

Sleep is a biological process in which the reaction of a living being toward surrounding changes becomes reduced [1]. It is necessary to regulate body functions as it is present in most organisms. Most recent research suggests that sleep facilitates removing the neural waste product and restores the brain's energy sources [2, 3]. Sleep efficiency refers to the ratio of total sleep to time in bed. A decreased sleep efficiency indicates insomnia and lack of sleep [4]. Sleep efficiency depends upon various factors, including aging. Sleep-related changes occur as the body functions lose their efficiency, along with disturbances in homeostasis and circadian rhythms [5].

Diabetes mellitus (DM) is a collection of disorders resulting in hyperglycemic conditions of the body. DM becomes chronic due to impairment of organ dysfunction for a long time, resulting in its failure. Smoking, obesity, aging, and an unhygienic diet are some of their triggering factors. Sleep efficiency could cause diabetes, inducing the negative outcomes of metabolism due to increased sympathetic activity. Hypertension, fat deposition, and disruption in metabolic processes will likely cause poor sleep efficiency [6]. A low level of sleep efficiency could worsen the symptoms of type 2 DM, and it could induce the prevalence of diabetes by disrupting glucose tolerance [7].

Arthritis is the inflammation of the joints due to the destruction of the cartilaginous joint surface, resulting in immobility and disability. Osteoarthritis and rheumatoid arthritis are two of their prevalent types. Rheumatoid arthritis (RA) is an autoimmune disorder that destroys the

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joint capsule. There is an increased occurrence of sleep disturbances in RA due to chronic pain and anxiety. Poor sleep quality could also enhance disease activity and reduce health-related quality of life [8]. According to Bjurström, Olmstead, and Irwin (2017), more than 60% of patients with RA tend to develop sleep irregularities. Another factor that could induce sleep disturbance is the increased interleukin-6 and tissue necrotic factor [9]. The role of medicines has also affected the sleep cycle negatively. Prednisone and endogenous glucocorticoids produce harmful effects that maintain their efficiency at optimum levels. Depression is also a major consequence of RA, and it is believed that it could be a source of Insomnia in RA patients [10].

The presence of two chronic disorders would have unfavorable consequences affecting the body's sleep homeostasis. Despite extensive research on the individual effects of DM and RA on sleep patterns, limited attention has been given to the combined impact of these two conditions on sleep efficiency variability. This study addresses that gap, aiming to uncover how comorbid DM and RA interact to disrupt sleep patterns. To guide the research, the following hypotheses were proposed:

H1: Patients with comorbid DM and RA exhibit greater sleep efficiency variability compared to those with DM or RA alone or healthy controls.
H2: The increased variability in sleep efficiency in patients with both conditions is mediated by physiological factors such as systemic inflammation and psychological factors like depression.

This research has been conducted to observe and analyze the data on the sleep efficiency variability of patients suffering from DM and RA for a long time. Both conditions have vulnerable effects on the body, leading to a weak psychological state and an exposed immune system [11, 12].

While previous literature has reported the individual effects of DM and RA on sleep, research on the combined impact of these two chronic diseases on sleep efficiency variability remains limited. This gap in knowledge underscores the importance of understanding how comorbid DM and RA impact sleep homeostasis and variability in sleep patterns. The present study aims to investigate the variability in sleep efficiency among patients suffering from both DM and RA. The objectives of this study are as follows:

- To assess whether comorbid DM and RA are associated with increased variability in sleep efficiency
- To examine the potential physiological and physiological mechanisms contributing to this variability

By addressing this gap, this study seeks to provide novel insights into how these conditions interact to influence sleep patterns, offering implications for better management strategies.

Method

Research Design

Midlife in the United States Second Wave Research (MIDUS-2) has guided this cross-sectional research. The MIDUS-2 is a national multi-site longitudinal research of health and well-being [13]. The main goal of MIDUS-2 is to assess how the factors related to behavior, psychology, and society contribute to the comprehension of age-related samples. There were three recruitment sites: Georgetown University, the University of Wisconsin, and the University of California Los Angeles. All participants provided informed consent, and Institutional Review Board (IRB) approval was obtained for each participating site. The data utilized in this study are deidentified, ensuring participant confidentiality.

Participants

More than 7000 participants were part of the preliminary research conducted by MIDUS in 1994. Follow-up research on MIDUS included 5900 participants and was called the MIDUS 2 sample. For this study, we included 434 (aged between 34 and 84 years) who had available sleep data. Deidentified data accessibility and design, sampling criteria, and methodology details are available at www.midus.wisc.edu/ and https://www.icpsr.umich.edu/web/NACDA/studies/29282/versions/V9 (Ryff, Seeman, & Weinstein, 2021). Participants were selected based on self-reported health conditions, particularly their responses to the following yes/no questions: "Have you ever been diagnosed with any of the following disorders/ conditions in your life?" Self-reported data on diabetes mellitus (DM) and rheumatoid arthritis (RA) were used to classify participants into four groups: (1) DM only, (2) RA only, (3) combined DM and RA, and (4) healthy (no DM and RA). Previous studies have validated the reliability of self-reported RA and DM diagnoses [14, 15].

Measures

The ratio of total minutes spent in bed asleep and the total minutes spent in bed awake (multiplied by 100) is the way to calculate sleep efficiency. Sleep efficiency was expressed as the percentage of time spent asleep while in bed, with higher values indicating better sleep quality. The variation of

Table 1 Participants' characteristics for all groups

	All participants	Healthy group	DM solo group	RA only group	Combined RA and DM	*p* value
Participants, *n* (%)	434	192 (44.23)	29 (0.06)	172 (39.63)	41 (0.09)	
Age, year (SD)	54.08 ± 11.63	50.21 ± 10.35	53.69 ± 10.49	56.77 ± 11.51	61.22 ± 12.40	0.12
Female, *n* (%)	265 (61.05)	118 (61.45)	16 (55.17)	105 (61.04)	26 (63.41)	0.91
BMI, kg/m^2 (SD)	30.64 ± 7.32	29.04 ± 6.22	29.90 ± 5.82	31.24 ± 7.74	36.16 ± 8.42	0.001
Number of chronic conditions, mean (SD)	4.11 ± 2.97	2.64 ± 2.33	4.24 ± 2.11	5.20 ± 2.56	7.56 ± 2.88	< 0.001
Sleep efficiency, mean (SD)	79.16 ± 10.56	81.55 ± 9.18	75.35 ± 11.43	78.37 ± 10.60	74.00 ± 12.87	0.001
Sleep efficiency variability, mean (SD)	9.96 ± 9.26	8.54 ± 7.91	13.01 ± 12.79	14.04 ± 9.35	14.12 ± 10.32	0.002
CESD > 16, *n* (%)	84 (19.35)	33 (17.18)	9 (31.03)	32 (18.60)	10 (24.39)	0.28
Blood hemoglobin A1c%, mean (SD)	6.19 ± 1.23	5.82 ± 0.50	8.11 ± 2.00	5.90 ± 0.52	7.84 ± 2.12	< 0.001
Number of prescribed medications, mean (SD)	2.78 ± 3.04	1.75 ± 2.35	4.34 ± 3.01	2.91 ± 3.06	5.90 ± 3.26	< 0.001

sleep efficiency was computed by the equation of coefficient of variance, which equals the ratio of (seven nights standard deviation of sleep efficiency and seven nights average of sleep efficiency) multiplied by 100. Increasing the number of sleep efficiency variability indicates a high variation of night-to-night sleep during an entire week.

The covariates in this research include age, gender, body mass index (BMI), depressive symptoms, and amount of prescribed medication. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CESD). Participants scoring ≥ 16 were classified as having depressive symptoms [16].

Statistical Analysis

Descriptive statistics included means for continuous variables and counts for categorical variables, summarized for all groups. The chi-square test was applied to evaluate the variance in population properties between groups for categorical data. The Kruskal–Wallis test was used for continuous variables due to the non-parametric nature of the data. These statistical tests were chosen to accommodate the skewness observed in the data.

Multiple linear regression analyses investigated the relationship between groups (combined RA and DM, DM solo, and RA only versus healthy) and sleep efficiency variability. The healthy group was chosen as the reference category compared to other groups, including DM solo, RA only, and combined DM and RA. Model 1 controlled for age and gender, while Model 2 included additional covariates: BMI, depressive symptoms, and prescribed medication use. The selection of the Kruskal–Wallis test and multiple linear regression analyses was based on their robustness in handling non-normally distributed data and controlling for confounding factors, respectively. A power analysis was conducted, revealing that the sample size of 434 participants provided sufficient statistical power (80%) to detect medium effect sizes (Cohen's $f^2 = 0.15$) at an alpha level of 0.05. Statistical analyses were performed using SPSS for Macintosh, version 25.0 (SPSS Inc., Chicago, IL). All statistical tests were conducted at a significance level of 0.05.

Results

There were a total of 434 participants analyzed. The average age of the whole sample was 54.08 ± 11.63, and the average BMI was 30.64 ± 7.32. Of the entire sample, 265 (61.05%) participants were females, while group distributions were as follows: 41 (9.45%) participants had both RA and DM, 172 (39.63%) participants had RA only, 29 (6.68%) participants had DM solo, and 192 (44.23%) were healthy participants. The differences in participants' demographics and characteristics when compared to the groups are shown in Table 1.

The average sleep efficiency significantly differed between groups ($p < 0.001$), with the combined RA and DM group demonstrating the lowest efficiency (74%), followed by DM also (75.35%), RA only (78.37%), and the healthy group (81.55%). BMI, sleep efficiency variability, number of comorbid conditions, glycemic control, and number of prescribed medications significantly differed between groups ($p < 0.001$).

Biological and psychosocial factors likely impact these differences. For example, participants with both RA and DM may experience higher systemic inflammation, joint pain, or neuropathy, disturbing sleep quality. Psychosocial stress from managing multiple chronic conditions can further exacerbate variability in sleep patterns.

Regression analysis further clarified these differences. In Table 2, the analysis of multiple linear regression indicates that combined RA and DM were significantly associated

Table 2 Linear regression analyses for the associations between groups and sleep variability

Groups	Model 1			Model 2		
	B	SE	*p* value	*B*	SE	*p* value
Combined RA and DM	6.45	1.60	< 0.001	5.14	1.79	0.004
DM solo	4.60	1.79	0.01	3.66	1.76	0.038
RA only	1.98	0.98	0.043	1.31	1.04	0.21
Healthy	Reference			Reference		
R	0.10			0.28		

Model 1: adjusted for age and sex

Model 2: adjusted for age, sex, body mass index, depression, and the number of prescribed medications

SE standard error

with increased variability of sleep efficiency ($B = 5.14$, 95% confidence interval (CI) (1.62 to 8.66), $p = 0.004$). However, RA alone showed a significant but less pronounced association ($B = 3.66$, 95% CI (0.20–7.12), $p = 0.038$), indicating that while RA contributes to sleep variability, the combined effect with DM is more substantial. This suggests that the comorbidity of RA and DM has a stronger clinical impact on sleep variability than either condition alone. DM solely was not significantly associated with increased variability in sleep efficiency ($B = 1.31$, 95% CI (-0.72 to 3.35), $p = 0.21$). The regression models were adjusted for age, gender, BMI, depressive symptoms, and the number of prescribed medications.

Discussion

Sleep deprivation imbalances the body's hemostasis, leading to multiple complications, such as metabolic dysfunction and hormonal imbalances. This can aggravate appetite and arousal at midnight [17]. Li et al. reported that a normal sleep efficiency should be 85%; values below this threshold indicate potential sleep issues [18]. Hormonal imbalances are major causes of sleep disturbances in aged persons. Melatonin is an important hormone regulating sleep rhythms that increase during nighttime but are reduced with age. Other hormones, including growth hormone, cortisol, and thyroid-stimulating hormone, also play important roles in regulating the human circadian rhythm [5].

This research investigates sleep efficiency in three different groups, including a control group, patients with diabetes mellitus (DM), patients with rheumatoid arthritis (RA), and those with both conditions. The findings of this study indicate that the patients with symptoms of both RA and DM had decreased sleep efficiency compared to other groups. Notably, patients with RA tend to have better sleep efficiency compared to diabetic patients. Previous research has suggested a link between irisin levels and poor sleep quality in individuals with a history of RA [19].

The regression analysis results suggest that the combined presence of DM and RA has a significant, clinically relevant impact on sleep efficiency variability. Patients with both conditions showed greater night-to-night variability in sleep efficiency, which is clinically important as it may indicate an increased risk of sleep-related health issues, including metabolic and cardiovascular problems. RA alone, while associated with increased sleep variability, exhibited a less pronounced effect, underscoring the compounded impact of having both conditions.

Engaging in physical activity may improve sleep quality by reducing inflammation markers such as interleukin-6 and tumor necrosis factor (TNF) [20]. However, this study did not include measures of physical activity or diet, which are known to influence sleep patterns and could be contributing factors to the observed variability in sleep efficiency. Future studies should consider including these variables to better capture the multifactorial nature of sleep disturbances.

The result of this study shows a great variation between the sleep efficiency of symptomatic and asymptomatic patients. Healthy individuals demonstrate a sleep efficiency exceeding 80%, whereas patients with RA often struggle with chronic pain, leading to alterations in their sleep patterns becoming a part of their daily lives [21]. Pain, mood disturbance, and disability are significantly impacted by sickness beliefs like helplessness and internality (perceived control) and pain coping techniques, according to a number of cross-sectional and longitudinal studies in the RA literature [22, 23]. Istle et al. found that 41.75% of RA patients had poor sleep quality, with anxiety and depression as key predictors. Similarly, our study highlights the role of depression in sleep disturbances, particularly in RA and DM comorbidities, where sleep efficiency was lowest [24].

Moreover, the psychosocial impact of chronic pain frequently results in depression, which is a significant factor influencing variations in sleep quality [25]. Research indicates that disease-modifying anti-rheumatic drugs (DMARDs) can also disrupt sleep patterns [8]. There is a well-established connection between sleep disturbances

and systemic diseases like RA and DM, which compromise the immune system and contribute to pain. Insufficient rest can diminish overall productivity and further impair bodily functions. Diabetes can lead to severe mental health issues alongside complications such as nephropathy and neuropathy, complicating symptom management. Sleep disturbances and anxiety may arise from dysfunctions in the frontal-limbic system, disrupting hypothalamic signaling to the pituitary and adrenal glands, ultimately leading to endocrine imbalances [26]. These findings highlight the importance of integrating sleep management into clinical practice for patients with both RA and DM to mitigate these adverse effects. Clinical interventions aimed at improving sleep efficiency could reduce the burden of these chronic diseases and improve patients' overall health outcomes.

Limitations

Although the study provides valuable insights, there are limitations to consider. First, the cross-sectional nature of the MIDUS-2 data limits causal inferences, as we cannot determine whether RA, DM, or their combination directly caused sleep disturbances. Longitudinal studies would better capture these dynamics. Second, the reliance on self-reported diagnoses could introduce bias, as participants may misclassify their symptoms or medical conditions. This lack of clinical verification is a notable limitation. Future studies should incorporate objective clinical assessments for validation. Third, the sample sizes for some groups (e.g., DM solo) were small, potentially limiting statistical power. Finally, external factors such as medication adherence, physical activity, or diet, which could influence sleep efficiency, were not controlled in this analysis.

Conclusion

Sleep efficiency indicates a healthy life with the body functioning with its total potential. Variation in sleep variability is generally caused due to any underlying disorder. This research has been conducted, planned with the help of MIDUS-2, to evaluate the effects of RA and DM, two chronic conditions, on sleep efficiency. Results show that patients experience trouble maintaining normal sleep efficiency due to systemic disorders and the negative effects of medications affecting their endocrine systems. There is a close relevance between variations in the sleep cycle and systemic conditions.

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Data Availability The data supporting this study's findings are derived from MIDUS research. Restrictions apply to the availability of these data, which were used under license for this study. Data are available at www.midus.wisc.edu/ and https://www.icpsr.umich.edu/web/NACDA/studies/29282/versions/V9.

Declarations

Competing Interests The author declares no competing interests.

References

1. Hobson JA. Sleep is of the brain, by the brain and for the brain. Nature. 2005;437(7063):1254–6.
2. Benington JH, Heller HC. Restoration of brain energy metabolism as the function of sleep. Prog Neurobiol. 1995;45(4):347–60.
3. Xie L, Xu Kang H, Q, et al. Sleep drives metabolite clearance from the adult brain. Science. 2013;342:373–8.
4. Reed DL, Sacco WP. Measuring sleep efficiency: what should the denominator be? J Clin Sleep Med. 2016;12(2):263–6.
5. Li J, Vitiello MV, Gooneratne NS. Sleep in normal aging. Sleep Med Clin. 2018;13(1):1–11.
6. Yan B, et al. The association between sleep efficiency and diabetes mellitus in community-dwelling individuals with or without sleep-disordered breathing. J Diabetes. 2020;12(3):215–23.
7. Arora T, et al. The impact of sleep debt on excess adiposity and insulin sensitivity in patients with early type 2 diabetes mellitus. J Clin Sleep Med. 2016;12(5):673–80.
8. Zhang L, Shen B, Liu S. Rheumatoid arthritis is associated with negatively variable impacts on domains of sleep disturbances: evidence from a systematic review and meta-analysis. Psychol Health Med. 2021;26(3):267–77.
9. Bjurström F, Olmstead R, Irwin MR. Reciprocal relationship between sleep macrostructure and evening-and morning cellular inflammation in rheumatoid arthritis. Psychosom Med. 2017;79(1):24.
10. Goes ACJ, et al. Rheumatoid arthritis and sleep quality. Rev Bras Reumatol. 2017;57:294–8.
11. Daryabor G, et al. The effects of type 2 diabetes mellitus on organ metabolism and the immune system. Front Immunol. 2020;11:1582.
12. Euesden J, et al. The relationship between mental health, disease severity, and genetic risk for depression in early rheumatoid arthritis. Psychosom Med. 2017;79(6):638.
13. Dienberg Love G, et al. Bioindicators in the MIDUS national study: protocol, measures, sample, and comparative context. J Aging Health. 2010;22(8):1059–80.
14. Schneider AL, et al. Validity and reliability of self-reported diabetes in the atherosclerosis risk in communities study. Am J Epidemiol. 2012;176(8):738–43.
15. Bombard JM, et al. Validity and reliability of self-reported arthritis: Georgia senior centers, 2000–2001. Am J Prev Med. 2005;28(3):251–8.

16. Barlow JH, Wright CC. Dimensions of the Center of Epidemiological Studies-Depression Scale for people with arthritis from the UK. Psychol Rep. 1998;83(3):915–9.
17. Lee SWH, Ng KY, Chin WK. The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: a systematic review and meta-analysis. Sleep Med Rev. 2017;31:91–101.
18. Li W, et al. Association between loss of sleep-specific waves and age, sleep efficiency, body mass index, and apnea-hypopnea index in human N3 sleep. Aging Dis. 2020;11(1):73.
19. Gamal RM, et al. Preliminary study of the association of serum irisin levels with poor sleep quality in rheumatoid arthritis patients. Sleep Med. 2020;67:71–6.
20. Boeselt T, et al. Sleep and rheumatic diseases. Best Pract Res Clin Rheumatol. 2019;33(3):101434.
21. Karstensen, J.K., et al. Lifestyle factors in patients with rheumatoid arthritis—a cross-sectional study on two Scandinavian cohorts. Clinical Rheumatol 2021: 1–12.
22. Brown GK, Nicassio PM. Development of a questionnaire for the assessment of active and passive coping strategies in chronic pain patients. Pain. 1987;31(1):53–64.
23. Nicassio PM, et al. The measurement of helplessness in rheumatoid arthritis. The development of the arthritis helplessness index. J Rheumatol. 1985;12(3):462–7.
24. Juárez-Rojop, I.E., et al. Prevalence of poor sleep quality and associated factors in individuals with rheumatoid arthritis: a cross-sectional study. Medicina (Kaunas), 2023. 59(9).
25. Lee S, et al. Factors that influence sleep disturbance and the mediating effects of depression on sleep disturbance in patients with rheumatoid arthritis. Orthop Nurs. 2022;41(5):335–44.
26. Kheirkhah, F., et al. Sleep quality and depression: does diabetes mellitus affect the association in older patients? Iranian Journal of Psychiatry Behav Sci. 2022; 16(2).