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Research Article

Fatigue, Nonrestorative Sleep and Associated Factors Among Sudanese Patients with Type 2 Diabetes: A Case-Control Study

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Abstract:

Background: Fatigue, nonrestorative sleep, and other sleep disorders could be pointers to serious medical problems like obstructive sleep apnea; when present in patients with diabetes, they exacerbate each other deleterious consequences. The present study aimed to assess fatigue, nonrestorative sleep, sleep duration, and daytime sleepiness among patients with type 2 diabetes.

Methods: This cross-sectional descriptive study was conducted among 103 consecutive patients with type 2 diabetes and 121 healthy controls attending an outpatient clinic in Omdurman, Sudan during the period from December 2015 to June 2016. All participants signed a written informed consent and were interviewed using a questionnaire based on Epworth Sleepiness Scale to assess subjective nonrestorative sleep, sleep duration, and snoring. A blood sample was taken for the HbA1c. The local ethical committee approved the research, and chi-square test and *t*-test were used for data analysis.

Results: Highly significant statistical differences were observed between the diabetic patients and the control subjects regarding fatigue, nonrestorative sleep, sleep duration, snoring, and excessive daytime sleepiness ($p < 0.001$). Patients with fatigue had higher nonrestorative sleep than those without, no significant differences were found between patients with the symptoms of fatigue and those without regarding excessive daytime sleepiness, snoring, sleep duration, and the HbA1c ($p > 0.05$).

Conclusions: Fatigue, nonrestorative sleep, sleep duration, excessive daytime sleepiness, and snoring were common among patients with type 2 diabetes than their healthy counterparts, diabetic patients with fatigue had more nonrestorative sleep than those without. The reliance on a self-administered questionnaire is a limitation of the study.

Key words: Fatigue, nonrestorative sleep, excessive daytime sleepiness, diabetes mellitus, Sudan

Introduction

Diabetes mellitus is a lifelong morbid disorder causing a lot of mortality and morbidity. Overall, 6% of the world population is affected by the disease, and the number is projected to reach 438 million by the year 2030. Currently, 7.7% of adult population is affected by diabetes mellitus in Sudan, and the level is rising at an alarming rate [1–3].

Chronic fatigue is common among patients with diabetes and can be reported in more than half of them. Fatigue can affect adversely the quality of life, compromise the self-management of diabetes, and increase complications that come with the disease. The pathophysiology of diabetes mellitus and fatigue could be shared in some respects [4, 5] (the release of inflammatory markers like Tumor Necrosis Factor, interleukins, and increased C-reactive proteins are to blame for both conditions).

Fatigue can be acute and fluctuating during the day or a chronic persistent with functional impairment. Hyperglycemia in patients with diabetes precipitates fatigue, while sleep disorders, depression, and pain perpetuate it [6–9].

Previous literature indicated a U-shaped relationship between diabetes and sleep with an increasing incidence among those who sleep less than six or more than eight hours per night [10]. Physiological studies have documented the activation of the autonomic nervous system and the hypothalamic-pituitary-adrenal axis leading to an increase in the heart rate and impairment of its variability among patients with insomnia who met the objective and subjective criteria during polysomnography. An increase in the metabolic rate was also observed in those patients [11–13]. Nonrestorative sleep is the subjective feeling of unrefreshing sleep, up to 10% of the healthy individuals could be affected by this disorder. Nonrestorative sleep may be associated with insomnia, unhealthy lifestyles, and gastroesophageal reflux disease [14, 15].

Excessive daytime sleepiness and snoring are clinical indicators of obstructive sleep apnea and have been linked to an increasing morbidity and mortality in various clinical setting including diabetes mellitus. Excessive daytime somnolence could impair diabetes self-management and increase the glycated hemoglobin and lead to higher rate of microvascular complications [16]. Not many researchers have studied fatigue, insomnia, and excessive daytime sleepiness in Sudan and the studies conducted on this factors in the Western countries may not apply to Sudan. Thus, the present research was conducted to assess fatigue, excessive daytime sleepiness, and insomnia among patients with type 2 diabetes mellitus in Sudan.

Materials and Methods

This case-control study was conducted among 102 consecutive patients with type 2 diabetes mellitus and 121 healthy controls during the period from December 2015 to June 2016. The participants were attending an outpatient diabetes clinic at the Omdurman Teaching Hospital, Omdurman, Sudan; the diabetic patients were chosen from amongst the regular follow-up patients, and the control subjects were chosen from

the relatives and co-patients to address the confounding factors like socioeconomic factors and level of education [17].

The sample size was calculated using the formula: $n = Z^2\ P - Q/d^2$, where Z = 95% confidence (1.96), P = Prevalence of diabetes mellitus in Sudan [3], Q = 100–prevalence, and d = tolerated error. All participants signed a written informed consent and were then interviewed using a structured questionnaire to collect demographic data on subjective sleep duration, non-restorative sleep during the past month, and fatigue that persisted during the day with the disturbance in function [6]. Those with chronic medical conditions like rheumatic disorders as well as those with psychological diagnosis, cigarettes smokers, and alcohol consumers were excluded. The Epworth Sleepiness Scale (ESS) was used [18] to assess patients' likelihood of falling asleep during the course of the day, the scale is an eight component choice questions with a total score of 24; these eight components are: how likely are you to fall asleep when: watching TV, sitting and reading, sitting inactively in public places, as a passenger in a car for one hour without a break, lying down to rest in the afternoon when circumstances permit, sitting talking to someone, sitting quietly after a lunch without alcohol, and in a car, while stopping for a few minutes in traffic. Each component is scored between 0 and 3 with 0 indicating no tendency for dosing off and 3 being severe dysfunction. A person who scores 10 or more is regarded as an excessive daytime sleeper. Weight and height were also measured, and the Body Mass Index (BMI) was measured using the formula: weight in kg/height in meter square. A BMI ≥ 30 was regarded as obesity, 25–29 as overweight, and 18–25 as normal. Blood sample was taken to assess the glycemic control (HbA1c%). The research was approved by the local ethical committee.

Data were analyzed using the statistical software (SPSS version 20), Chi-square test, and *t*-test and $P < 0.05$ was considered as statistically significant.

Results

Overall, 102 patients with type 2 diabetes and 121 control subjects were included in the study, with ages 58.39 ± 8.74 and 50.58 ± 10.17 years, respectively, $p < 0.001$; female dominance was apparent in both patients (71.6%) and controls (64.5%), $p = 0.314$; fatigue was reported in the majority of the patients (70.5% vs 36.3% among control subjects) with a high significant statistical difference, $p < 0.001$; non-restorative sleep was evident in 91.1% of the patients and 74.3% of the controls with a significant statistical difference, $p = 0.001$; while regular snoring was found in 56.9% and 28.1% of patients and controls, respectively, $p < 0.001$. Table 1 shows the comparison between patients with type 2

Table 1: Comparison Between Patients with Type 2 Diabetes and Control Subjects.

Characteristics	Diabetic Patients	Control Subjects	*p* value*
Sex			0.314
Males	29 (28.4%)	43 (35.5%)	
Females	73 (71.6%)	78 (64.5%)	
Regular snoring	58 (56.9%)	34 (28.1%)	0.000
Non-restorative sleep	93 (91.1%)	90 (74.3%)	0.001
Fatigue	72 (70.5%)	44 (36.3%)	0.000
Excessive daytime sleepiness	41 (40.2%)	13 (10.7%)	0.000
Sleeping hours			
<6 hours/night	57 (55.9%)	18 (14.9%)	0.000
Mean ± SD	5.29 ± 1.20	5.29 ± 1.20	

*Chi-square test

Table 2: A Comparison Between Diabetic Patients with and Without Fatigue.

Characteristics	Fatigue Present	Fatigue Not Present	*p* value*
Sex			0.461
Males	22 (30.5%)	7 (23.3%)	
Females	50 (69.5%)	23 (76.6%)	
Snoring	42 (58.3%)	16 (53.3%)	0.666
Non-restorative sleep	71 (98.6%)	22 (73.3%)	0.000

*Chi-square

Table 3: T-Test Comparing Diabetic Patients with and Without Fatigue.

Characteristics	Fatigue Present	Fatigue Not Present	*p* value*
Age	58.01 ± 8.84	59.30 ± 8.59	0.501
Daytime sleepiness	7.37 ± 5.11	7.23 ± 4.39	0.895
HbA1c	9.44 ± 1.88	8.89 ± 1.90	0.186
BMI	31.50 ± 4.80	30.00 ± 4.16	0.139
Sleep duration	5.30 ± 1.26	5.26 ± 1.04	0.882

**T*-test

diabetes and healthy control subjects. Table 2 illustrates a comparison between patients with and without fatigue in which snoring was found in 58.3% of the diabetic patients with fatigue and 53.3% of their counterparts with no significant statistical difference, $p = 0.666$; non-restorative sleep was higher among patients with fatigue at 98.6% vs 73.3% in controls with a high significant statistical difference, $p < 0.001$. As shown in Table 3, no significant differences were found between the diabetic patients with chronic fatigue and those without the abnormality regarding age (58.01 ± 8.84 vs 59.30 ± 8.59, $p = 0.501$), excessive daytime sleepiness (7.37 ± 5.11 vs 7.23 ± 4.39, $p = 0.895$), the HbA1c (9.44 ± 1.88 vs 8.89 ± 1.90, $p = 0.186$), BMI (31.50 ± 4.80 vs 30.00 ± 4.16, $p = 0.139$), and sleep duration (5.30 ± 1.26 vs 5.26 ± 1.04, $p = 0.882$).

Discussion

In the present study, majority of the patients with diabetes mellitus presented with fatigue and non-restorative sleep with a highly significant statistical difference between the patients and control subjects. Patients with type 2 diabetes mellitus had shorter sleep duration than controls and patients with chronic fatigue had higher non-restorative sleep than others without the diagnosis, while no significant difference was found between the two groups regarding the HbA1c, excessive daytime sleepiness, body mass index, and the duration of sleep.

There are complex discrepancies between causes and indicators of fatigue, so it's hard to define fatigue or transform it into a quantifiable measure. Due to the complex management strategies in diabetes, the importance of fatigue may be greater. In the present study, fatigue was more common among patients with type 2 diabetes than the healthy control subjects (70.5% vs 36.3%) in line with previous observations [19]. Another epidemiological study concluded fatigue in 61% of patients with type 2 diabetes, also in line with the current observations [20].

Various physiological and pathological disorders associated with diabetes mellitus like hyperglycemia, hypoglycemia, neuropathic pain, polypharmacy, and sleep disorders may result in fatigue [21–23]. Irrespective of the cause of death, both short and long sleep durations were associated with an increasing mortality. The growing rate of death might be free of diabetes and hypertension [24], in the current data, patients with type 2 diabetes mellitus slept for a short period and had a non-restorative sleep more than the controls, as in the Cespedes et al.'s study, who concluded the association between diabetes mellitus, short sleep duration, and insomnia [25].

Nonrestorative sleep may be a potential risk for various clinical outcomes related to sleep disorders even in the general population. However, factors involving nonrestorative sleep remain to be elucidated. Recent literature concluded the association of nonrestorative sleep with insomnia, psychiatric disorders, and gastroesophageal reflux disease [26]. In the present study, non-restorative sleep was present in 91.1% of patients with type 2 diabetes mellitus and 74.3% of control subjects with highly significant statistical difference; similarly, a study conducted among patients with the metabolic syndrome concluded the high rate of non-restorative sleep [27]. However, the relationship between fatigue and non-restorative sleep remains significant after controlling for age, sex, BMI, snoring, and excessive daytime sleepiness. The present observation calls for further larger multicenter studies to assess further possible

consequences of nonrestorative sleep among patients with type 2 diabetes mellitus in general and particularly those who present with the symptoms of fatigue.

Excessive daytime sleepiness and snoring are predictors of obstructive sleep apnea, a common sleep problem among patients with type 2 diabetes which when co-exist might increase each other's deleterious consequences [28]. In the present study, snoring and excessive daytime sleepiness were evident in 56.9% and 40.2% of diabetic patients with a high significant statistical difference between patients and control subjects similar to Kelly et al. [29] who found daytime sleepiness in 56% of hospitalized diabetic patients. Similarly, Marchiseni et al. [30] reported habitual snoring in 56.1% of obese patients. Fatigue could be a result of increasing BMI or lack of physical activity, but we did not assess the level of exercise as an important factor [31]. Also, we did not study other important factors like depression and diabetes distress that could contribute to the symptom of fatigue.

Conclusion

The present study concluded a high rate of fatigue, non-restorative sleep, short sleep duration, snoring and excessive daytime sleepiness, and a highly significant statistical relation between fatigue and non-restorative sleep. More larger studies using objective measure for the diagnosis of obstructive sleep apnea and assessing various possible causes of non-restorative sleep need to be conducted to improve diabetes care and quality of life because the above factors could impair the diabetes complex self-management.

Declaration: The views expressed in the submitted article are author's own and not an official position of the institution or funder.

Authors Contribution

- Concept and design: Dr. Hyder Mirghani
- Data collection: Dr. Hyder Mirghani and Dr. Fathiya
- Data analysis: Dr. Hyder Mirghani
- Manuscript drafting and critical revision for important intellectual content: Dr. Hyder Mirghani

References

[1] Acharya KG, Shah KN, Solanki ND et al. (2013). Evaluation of antidiabetic prescriptions, cost and adherence to treatment guidelines: a prospective, cross-sectional study at a tertiary care teaching hospital. *Journal of Basic and Clinical Pharmacy.* 4(4): 82–87.

[2] World Health Organization (1985). *Diabetes Mellitus: Report of a WHO Study Group* (Tech Report Ser No. 727). Geneva: World Health Organization.

[3] International Diabetes Federation (2015). *IDF Diabetes Atlas,* 7th edition. Middle East and North Africa.

[4] Lasselin J, Layé S, Dexpert S et al. (2012). Fatigue symptoms relate to systemic inflammation in patients with type 2 diabetes. *Brain, Behavior, and Immunity*. 26(8): 1211–1219. DOI: 10.1016/j.bbi.2012.03.003

[5] Martine MG, Cees JT, Elles S et al. (2014). Chronic fatigue in type1 diabetes: highly prevalent but not explained by hyperglycemia or glucose variability. *Diabetes Care.* 37(1): 73–80.

[6] Fukuda K, Straus SE, Hickie I et al. (1994). The chronic fatigue syndrome: a comprehensive approach to its definition and study. *Annals of Internal Medicine.* 121(12): 953–959.

[7] Reeves WC, Lloyd A, Vernon SD et al. (2003). Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution. *BMC Health Services Research.* 3(1): 25.

[8] Weijman I, Ros WJ, Rutten GE et al. (2005). Frequency and perceived burden of diabetes self-management activities in employees with insulin-treated diabetes: relationships with health outcomes. *Diabetes Research and Clinical Practice.* 68(1): 56–64.

[9] Hewlett S, Chalder T, Choy E et al. (2011). Fatigue in rheumatoid arthritis: time for a conceptual model. *Rheumatology*. 50(6): 1004–1006.

[10] Ayas NT, White DP, Al-Delaimy WK et al. (2003). A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care*. 26(2): 380–384.

[11] Vgontzas AN, Bixler EO, Lin HM et al. (2001). Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications.*Journal of Clinical Endocrinology & Metabolism.* 86(8): 3787–3794.

[12] Stepanski E, Glinn M, Zorick F et al. (1994). Heart rate changes in chronic insomnia. *Stress Medicine.* 10(4): 261–266.

[13] Bonnet MH, Arand DL (1995). 24-hour metabolic rate in insomniacs and matched normal sleepers. *Sleep.* 18(7): 581–588.

[14] Vernon MK, Dugar A, Revicki D et al. (2010). Measurement of non-restorative sleep in insomnia: a review of the literature. *Sleep Medicine Reviews*. 14(3): 205–212. DOI: 10.1016/j.smrv.2009.10.002

[15] Sarsour K, Van Brunt DL, Johnston JA et al. (2010). Associations of nonrestorative sleep with insomnia, depression, and daytime function. *Stress Medicine.* 11(10): 965–972. DOI: 10.1016/j.sleep.2010.08.007

[16] Mirghani HO, Merghani TH, Saadalla AM et al. (2016). Daytime sleepiness and chronic sleep deprivation in patients with type II diabetes mellitus and their relation o diabetic control. *Basic Research Journal of Medicine and Clinical Sciences*. 5(1): 12–16.

[17] Shehatah A, Rabie MA, Al-Shahry A (2010). Prevalence and correlates of depressive disorders in elderly with type-2 diabetes in primary health care settings. *Journal of Affective Disorders.* 123(1–3): 197–201.

[18] Johns MW (1999). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 14(6): 540–545.

[19] Singh R, Kluding PM (2013). Fatigue and related factors in people with type 2 diabetes. *The Diabetes Educator.* 39(3): 320–326. DOI: 10.1177/0145721713479144

[20] Drivsholm T, de Fine Olivarius N, Nielsen AB et al. (2005). Symptoms, signs and complications in newly diagnosed type 2 diabetic patients, and their relationship to glycaemia, blood pressure and weight. *Diabetologia*. 48(2): 210–214.

[21] Weijman I, Kant I, Swaen GM (2004). Diabetes, employment and fatigue-related complaints: a comparison between diabetic employees, “healthy” employees, and employees with other chronic diseases. *Journal of Occupational and Environmental Medicine.* 46(8): 828–836.

[22] McCormick M, Quinn L (2002). Treatment of type 2 diabetes mellitus: pharmacologic intervention. *Journal of Cardiovascular Nursing.* 16(2): 55–67.

[23] Resnick HE, Redline S, Shahar E (2003). Diabetes and sleep disturbances: findings from the Sleep Heart Health Study. *Diabetes Care.* 26(3): 702–709.

[24] Ikehara S, Iso H, Date C et al. (2009). Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study. *Sleep.* 32(3): 295–301.

[25] Cespedes EM, Dudley KA, Sotres-Alvarez D et al. (2016). Joint associations of insomnia and sleep duration with prevalent diabetes: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *Journal of Diabetes.* 18(3): 387–397. DOI:10.1111/1753-0407.12308

[26] Matsumoto T, Tabara Y, Murase K et al. (2017). Combined association of clinical and lifestyle factors with non-restorative sleep: The Nagahama Study. *PLOS ONE.* 2(3): e0171849. DOI:10.1371/journal.pone.0171849

[27] Hasan A, Uzma N, Swamy TL et al. (2012). Correlation of clinical profiles with obstructive sleep apnea and metabolic syndrome. *Sleep Breath.* 16(1): 111–116. DOI:10.1007/s11325-010-0463-z

[28] Mirghani HO, Elbadawi AS (2016). Depression, anxiety, and daytime sleepiness among type 2 diabetic patients and their correlation with the diabetes control: a case-control. *Journal of Taibah University Medical Sciences.* 11(4): 374–379.

[29] Kelly E, Cullen G, McGurk C (2007). Obstructive sleep apnea in patients with type 2 diabetes. *Thorax.* 62: 651.

[30] Marchiseni G, Pontiroli A, Salvioli G et al. (2004). Snoring, hypertension and Type 2 diabetes in obesity. Protection by physical activity. *Journal of Endocrinological Investigation.* 27(2): 150–157.

[31] Telford RD (2007). Low physical activity and obesity: causes of chronic disease or simply predictors? *Medicine & Science in Sports & Exercise*. 39(8): 1233–1240.