Table 3 Results of logistic regression analyses

	Crude OR	95% CI	*P*-value	Adjusted OR	95% CI	*P*-value
Gender			0.31			
Male	1.00					
Female	0.56	0.18–1.75				
Age classification (years)			0.37			
<50	0.62	0.06–6.19				
50–59	0.44	0.07–2.71				
60–69	1.11	0.27–4.57				
70≤	1.00					
BMI			0.65			
<25	1.00					
≥25	1.33	0.39–4.50				
Systolic blood pressure			0.02			0.07
<130	1.00			1.00		
≥130	4.19	1.12–15.70		3.64	0.91–14.61	
Smoking			0.10			
No	1.00					
Yes	1.01	0.22–4.71				
Exercise			0.99			0.08
No	2.60	0.81–8.37		3.20	0.87–11.79	
Yes	1.00			1.00		
Sleep disorder						
Difficulty initiating sleep			<0.01			0.01
No	1.00			1.00		
Yes	6.54	2.02–21.18		5.27	1.48–18.77	
Difficulty remaining alert			0.65			
No	1.00					
Yes	1.62	0.20–13.15				
Difficulty maintaining sleep			0.02			
No	1.00					
Yes	3.65	1.15–11.60				
Use of hypnotic medication			0.54			
No	1.00					
Yes	1.90	0.23–15.45				
Going to the restroom during night		0.15				
No	1.00					
Yes	2.30	0.72–7.42				
Having pain			0.69			
No	1.00					
Yes	1.53	0.19–12.40				
Sleep duration (h)			0.10			0.56
<8	1.00			1.00		
8 to <9	3.50	0.71–17.19		4.30	0.81–22.88	
≥9	3.50	0.49–18.43		2.53	0.36–17.74	
CES-D			0.05			0.08
<16	1.00			1.00		
≥16	3.26	1.01–10.54		3.28	0.86–12.46	
High-density lipoprotein cholesterol level			0.47			
<40	1.00					
≥40	2.14	0.26–17.53				
Triglyceride level			0.06			
<150	1.00					
≥150	3.42	0.89–13.20				

BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; OR, odds ratio. Variables excluded by the process of backward elimination analysis are represented by an empty column.

Table 4 Results of logistic regression analyses by gender

	Crude OR	95% CI	*P*-value	Adjusted OR	95% CI	*P*-value
Males						
Difficulty initiating sleep			0.04			
No	1.00					
Yes	5.48	1.04–28.83				
Females						
Difficulty initiating sleep			0.01			0.02
No	1.00			1.00		
Yes	8.60	1.53–48.27		7.91	1.38–45.42	

CI, confidence interval; OR, odds ratio. Males: Multivariate logistic regression analyses were conducted with adjustment for age, body mass index, systolic blood pressure, smoking, exercise, difficulty initiating sleep, difficulty maintaining sleep, going to the restroom during night, having pain, sleep duration, Center for Epidemiologic Studies Depression Scale (CES-D), triglyceride level. Females: Multivariate logistic regression analyses were conducted with adjustment for age, body mass index, smoking, exercise, difficulty initiating sleep, difficulty remaining alert, difficulty maintaining sleep, use of hypnotic medication, going to the restroom during night, sleep duration, Center for Epidemiologic Studies Depression Scale (CES-D), high-density lipoprotein cholesterol level, triglyceride level. Variables excluded by the process of backward elimination analysis are represented by an empty column.

results of our study are in agreement with those previous studies. Moreover, gender-specific analyses revealed significantly high odds ratios between new onset of hyperglycemia and difficulty in initiating sleep for both men and women in univariate analysis, and a significantly high odds ratio only for women in multivariate analysis. It is unclear why no significant association was observed in men in the multivariate analysis. This may be attributed to a small sample size, as a result of dividing the samples by gender, which may have lowered the statistical power. There is no medical consensus on whether there are gender-based differences with regard to associations between insomnia symptoms and impaired glucose tolerance. However, there may be gender-based differences with regard to endocrine metabolic functions for sleep.

Recent studies[38,39] have revealed that depression could be a confounding factor in the association between hyperglycemia and sleep disorders. However, the above-mentioned studies did not adjust for the depression status in their analyses; in contrast, in the present study, depression status was used as a covariate. Our results suggest that difficulty in initiating sleep is a risk factor for high fasting plasma glucose levels. We believe that the results of our study, which were obtained after adjustment for depression status, further support those of previous studies.

In our follow-up survey, we used a fasting plasma glucose level of ≥100 mg/dL as the reference level for impaired glucose tolerance, instead of using the one used as a diagnostic criterion for diabetes mellitus. A fasting plasma glucose level of ≥100 mg/dL indicated that the patient was in a prediabetic state. The results of our study suggest that sleeping disorders such as difficulty in initiating sleep affect plasma glucose levels in some people who are in a prediabetic state.

The present study results showed that compared to other insomnia symptoms and short sleep duration, difficulty in initiating sleep had a stronger association with impaired glucose tolerance. To date, associations between difficulty in initiating sleep and onset of impaired glucose tolerance have not been sufficiently examined either epidemiologically or physiologically in previous studies. Thus, the mechanism cannot be fully explained at this point. For further clarification of the association between insomnia and impaired glucose tolerance, more epidemiological studies must be conducted with different study populations, and meta-analyses of the results must be performed. We expect that such studies will help in determining good sleep habits and contribute to the prevention and treatment of diabetes mellitus. In addition, such findings will be conducive to healthcare and prevention activities and clinical practice in general.

There were several limitations to the present study. First, self-reported questionnaires were used to obtain data on sleep duration. Therefore, the data obtained were not objective. However, some studies have reported that self-reported data on sleep status do concur, to a certain extent, with physiologic data.[40,41] Second, although consumption of beverages such as alcohol and coffee, improper eating habits, and family history[12,13,42,43] are considered to be risk factors for diabetes mellitus, this study did not adjust for these factors.

Third, we only analyzed the cumulative incidence of hyperglycemia at 2 years among subjects who experienced difficulty in initiating sleep at the baseline survey; therefore, the changes in the plasma glucose levels during the period between the baseline and follow-up surveys could not be determined. Fourth, residents of a particular local community in Japan were used as samples in this study, and the sample size was small; the distributions of gender and age were not considered. Thus, the representativeness of the sampling was not ensured. Additionally, the small sample size made it impossible to use commonly used classifications for routine exercising and sleep duration. Fifth, because data on restless legs syndrome and sleep apnea were not collected, these were not considered in the analyses. Sixth, the possibility of a difference between the groups of participants and non-participants in the follow-up survey cannot be ruled out. However, a comparison between people who had participated only in the baseline survey and those who participated in both baseline and follow-up surveys showed no statistically significant difference in gender composition and the average age of participants in the baseline survey. This may signify that people who dropped out did not belong to any particular age group or gender.

Conclusions

The results of our prospective study conducted on residents of a local Japanese community suggest that difficulty in initiating sleep might be a risk factor for hyperglycemia 2 years after first experiencing sleep disturbance. These results will help in the formulation of guidelines for future preventive medicine practices such as healthcare education and guidance for local communities.

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REFERENCES

1 Klein S, Sheard NF, Pi-Sunyer X *et al.* Weight management through lifestyle modification for the prevention and management of type 2 diabetes: Rationale and strategies. *Diabetes Care* 2004; **27:** 2067–73.
2 Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution and weight gain as a risk factor for clinical diabetes in men. *Diabetes Care* 1994; **17:** 961–9.
3 Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes in women. *Ann. Intern. Med.* 1995; **122:** 481–6.
4 Petersen K, Beffoy D, Dufour S *et al.* Mitochondorial dysfunction in the elderly: Possible role in insulin resistance. *Science* 2003; **300:** 1140–2.
5 Hu FB, Manson JE, Stampfer MJ *et al.* Diet, lifestyle and the risk factor of type2 diabetes mellitus in women. *N. Eng. J. Med.* 2001; **345:** 790–7.
6 Waki K, Noda M, Sasaki S *et al.*; JPHC Study Group. Alcohol consumption and other risk factors for self-reported diabetes among middle-aged Japanese: a population-based prospective study in the JPHC study cohort I. *Diabet. Med.* 2005; **22:** 323–31.
7 Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Effects of smoking on the incidence of non-insulin dependent diabetes mellitus: replication and extension in a Japanese cohort of male employees. *Am. J. Epidemiol.* 1997; **145:** 103–9.
8 Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS Jr. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N. Engl. J. Med.* 1991; **325:** 147–52.
9 Manson JE, Rimm EB, Stampfer MJ *et al.* Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 1991; **338:** 774–8.
10 Manson JE, Nathan DM, Krolewski AS, Stampfer MJ, Willett WC, Hennekens CH. A prospective study of exercise and incidence of diabetes among US male physicians. *JAMA* 1992; **268:** 63–7.
11 Salmeron J, Ascherio A, Rimm EB *et al.* Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 1997; **20:** 545–50.
12 Marshall JA, Bessesen DH, Hamman RF. High saturated fat and low starch and fiber are associated with hyperinsulinaemia in a non-diabetic population: the San Luis Valley diabetes study. *Diabetologia* 1997; **40:** 430–8.
13 Lindstrom J, Peltonen M, Eriksson G *et al.* High-fiber, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study. *Diabetologia* 2006; **49:** 912–20.
14 Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a rised factor for the development of type2 diabetes. *Diabetes Care* 2006; **29:** 657–61.
15 Ayas NT, White DP, Al-Delaimy WK *et al.* A prospective study self-reported sleep duration and incident diabetes in women. *Diabetes Care* 2003; **26:** 380–4.
16 Meisinger C, Heier M, Loewel H. The MONICA/KARA Augsburg Cohort study. Sleep disturbance as a predictor of type2 diabetes mellitus in men and women from the general population. *Diabetologia* 2005; **48:** 235–41.

17 Mallon L, Broman JE, 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**: 2762–7.
18 Nilsson PM, Roost M, Engstrom G, Hedblad B, Berglunc G. Incidence of diabetes in middle-aged men is related to sleep disturbances. *Diabetes Care* 2004; **27**: 2464–9.
19 Vgontzas AN, Bixler EO, Lin H *et al.* Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications. *J. Clin. Endocrinol. Metab.* 2001; **86**: 3787–94.
20 Hjemdahil P. Stress and metabolic syndrome. *Circulation* 2002; **106**: 2634–6.
21 Spiegel K, Leproult R, Cauter EV. Impact of sleep debt on metabolic and endocrine function. *Lancet* 1999; **354** (23): 1435–9.
22 Spiegel K, Knutson K, Leproult R, Tasali E, Cauter EV. Sleep loss: a novel risk factor for insulin resistance and type2 diabetes. *J. Appl. Physiol.* 2005; **99**: 2008–19.
23 Gislason T, Almqvist M. Somatic diseases and sleep complaints: an epidemiological study of 3201 Swedish men. *Acta Med. Scand.* 1987; **221**: 475–81.
24 Markku T, Hyyppa EK. Quality of sleep and chronic illnesses. *J. Clin. Epidemiol.* 1989; **42**: 633–8.
25 Gottlieb DJ, Punjabi NM, Newman AB *et al.* Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch. Intern. Med.* 2005; **165**: APR25.
26 Nakajima H, Kaneita Y, Yokoyama E *et al.* Association between sleep duration and hemoglobin A1c level. *Sleep Med.* 2008; **9**: 745–52.
27 Kawakami N, Takatsuka N, Shimizu H. Sleep disturbance and onset of type 2 diabetes. *Diabetes Care* 2004; **27**: 282–3.
28 Hayashino Y, Fukuhara S, Suzukamo Y, Okamura T, Tanaka T, Ueshima H, for the HIPOP-OHP Research group. Relation between sleep quality and quantity, quality of life, and risk of developing diabetes in healthy workers in Japan: the High-risk and Population Strategy for Occupational Health Promotion (HIPOP-OHP) Study. *BMC Public Health* 2007; **7**: 129.
29 Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl. Psychol. Meas.* 1977; **1**: 385–401.
30 Shima S, Shikano T, Kitamura T, Asai M. A new self-rating scale for depression (in Japanese). *Clin. Psychiatry* 1985; **27**: 717–23.
31 Genuth S, Alberti KG, Bennett P *et al.*; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003; **26**: 3160–7.
32 The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003; **26**: 3160–7.
33 Irwin M, Clark C, Kennedy B, Gillin JC, Ziegler M. Nocturnal catecholamines and immune function in insomniacs, depressed patients, and control subjects. *Brain Behav. Immun.* 2003; **17**: 365–72.
34 Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Med.* 2004; **1**: e62.
35 Spiegel K, Leproult R, L'Hermite-Baleriaux M, Copinschi G, Penev P, Van Cauter E. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. *J. Clin. Endocrinol. Metab.* 2004; **89**: 5762–71.
36 Spiegel K, Tasali E, Penev P, Van Cauter E. Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels and increased hunger and appetite. *Ann. Intern. Med.* 2004; **141**: 846–50.
37 Antoine A, Lecea L. Sleep and metabolism: shared circuits, new connections. Trends in Endocrinology and. *Metabolism* 2008; **19**: 362–70.
38 Knol MJ, Twisk JWR, Beekman ATF, Heine RJ, Snoek FJ, Pouwer F. Depression as a risk factor for the onset of type2 diabetes: a meta-analysis. *Diabetologia* 2006; **49**: 837–45.
39 Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? *JAMA* 1989; **262**: 1479–84.
40 Hoch CC, Reynolds CF, Kupfer DJ *et al.* Empirical note :self-report versus recorded sleep in healthy seniors. *Psychiatry* 1987; **24**: 293–9.
41 Frankel BL, Coursey RD, Buchbinder R *et al.* Recorded and reported sleep in chronic primary insomnia. *Arch. Gen. Psychiatry* 1976; **33**: 615–23.
42 van Dam RM, Frank BH. Consumption and risk of type2 diabetes mellitus. *JAMA* 2005; **294**: 97–104.
43 Koppes LLJ, Dekker JM, Hendriks HFJ, Bouter LM, Heine RJ. Moderate alcohol consumption lowers the risk of type2 diabetes. *Diabetes Care* 2005; **28**: 719–25.