What is the Incidence of Sleep Apnea in Type 2 Diabetics in Japan?

—JEDAS Study Report— (JEDAS: Japanese Epidemiology DM and SAS)

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Comprehensive Support Project

Background

1. Stress associated with sleep apnea syndrome (SAS) has recently been brought to attention as a risk factor for abnormal glucose metabolism and insulin resistance. (Naresh *et al*. Am J Epidemiol, 2004)
2. Compared with non-diabetics, prevalence of SAS is known to be higher in diabetics in the U.S.A. and Europe (15.6% vs 23.8%). (Resnick *et al*. Diabetes Care, 2003) In contrast, SAS prevalence among Japanese diabetics is unknown.
3. SAS is strongly associated with obesity. A large percentage of Japanese type 2 diabetics is leptosomatic compared with their counterparts in the U.S.A. and Europe
4. We conducted a multicenter cross-sectional epidemiological study in outpatients with type II DM to estimate the prevalence of SAS among DM.

Objective

1. To estimate prevalence of SAS among type 2 diabetics
2. To explore association between SAS and diabetic pathology such as insulin resistance in type 2 diabetics

Materials & Method

Subjects

- Inclusion criteria: outpatients with type 2 diabetes (according to the diagnostic criteria of Japan Diabetes Society)
- Exclusion criteria: patients without diabetes treatment information for the last 3 months
- Number of patients analyzed: consecutive 904 patients

Study design

- Multicenter prospective cross-sectional observational study (epidemiological study)

Measurements/data investigated

- Demographic data, history of diabetes, physical measurements, vital signs, blood biochemical test (ex. FBG, fasting insulin, HbA_{1c}), urine test, lifestyle, past/current disorders and complications
- Nocturnal pulse oximetry to estimate presence of SAS
- Patient questionnaire (SF-36, Beck Depression Inventory, stress check list, Pittsburgh sleep quality index)

Statistical analysis

- Ratio estimation (95% CI), correlation analysis, multivariate analysis (ex. logistic regression)

Characteristics of the patients

Item	Male N	Male			Female N	Female		
Age (year)	602	60.6	±	12.3	302	62.7	±	11.5
Duration of diabetes (month)	552	128	±	107	262	119	±	98
Height (cm)	572	167.4	±	6.4	277	154.0	±	5.7
Weight (kg)	599	70.3	±	13.6	301	61.0	±	12.3
BMI (kg/m²)	572	25.0	±	4.3	277	25.6	±	4.7
Systolic BP (mmHg)	596	132	±	17	300	131	±	16
Diastolic BP (mmHg)	597	77	±	11	300	74	±	11
Heart rate (bpm)	502	77	±	12	236	78	±	12
Abdominal circumference (cm)	558	88.8	±	10.2	280	86.4	±	12.6
Fasting blood glucose (mg/dL)	314	139	±	47	151	134	±	40
Fasting insulin (μU/mL)	136	8	±	6	54	9	±	4
HbA1c (%)	593	6.9	±	1.2	292	6.9	±	1.1
HOMA-IR (IU/L)*	115	2.8	±	2.1	48	2.9	±	1.6
Creatinine (mg/dL)	583	0.83	±	0.22	291	0.66	±	0.39
3% ODI (/hour)	602	11	±	11	302	9	±	8
Number of diabetic complication**								
0	247				102			
1	123				53			
2	57				38			
3	44				16			

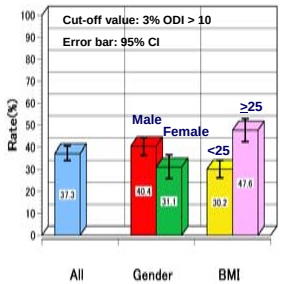
(Mean ± SD)

*Data of patients without previous insulin therapy

**Three major complications (diabetic retinopathy, diabetic nephropathy, diabetic neuropathy)

Result

Estimated SAS Prevalence



Simple Correlation with 3% ODI

Item	Correlation coefficient	P value	N
Height	0.07	0.05	849
Weight	0.23	<0.01	900
BMI	0.24	<0.01	849
Abdominal circumference	0.30	<0.01	818
Hip circumference	0.24	<0.01	818
Neck circumference	0.25	<0.01	818
Number of years drinking	0.08	0.04	627
Number of complication	0.11	<0.01	678
Fasting insulin	0.18	0.01	190
HOMA-IR (without previous insulin therapy)	0.17	0.03	163
Uric acid	0.13	<0.01	739
Creatinine	0.07	0.03	874
Systolic BP	0.12	<0.01	896
Diastolic BP	0.13	<0.01	897
Heart rate	0.09	0.01	738
Physical function	-0.12	<0.01	899

Multivariate Analysis Model (proportional odds model)

Statistically significant explanatory variables (statistical significance based on outcome variables categorized by SAS severity [3% ODI of < 5, 5 < and < 15 or 15 <])

Explanatory variable	Estimate	SE	P value	Odds ratio	95% CI	
Age	0.02	0.01	<0.01	1.02	1.01	1.04
Sex	-0.44	0.17	0.01	0.64	0.46	0.90
BMI	0.14	0.02	<0.01	1.15	1.11	1.20
Heart rate	0.01	0.01	0.03	1.01	1.00	1.03
Creatinine	0.86	0.34	0.01	2.37	1.21	4.65
Hypertension	0.42	0.15	0.01	1.52	1.13	2.03

Odds ratio per explanatory variable unit

Explanatory variable	Unit	Odds ratio	95% CI	
Age	10	1.27	1.12	1.45
Sex	Male vs Female	0.64	0.46	0.90
BMI	5	2.01	1.65	2.46
Heart rate	10	1.14	1.01	1.28
Creatinine	0.5	1.54	1.10	2.16
Hypertension	Yes vs NO	1.52	1.13	2.03

Summary

1. Estimated SAS prevalence among diabetics was 37.3% (95% CI, 0.34 to 0.41) with a cut-off value of 3% ODI > 10.
2. Estimated SAS prevalence among diabetics with BMI < 25 was 30.2% (95% CI, 0.26 to 0.34) with a cut-off value of 3% ODI > 10.
3. Correlation with SAS severity (3% ODI) was seen in (1) physique data (height, weight, BMI, abdominal circumference, hip circumference, neck circumference, number of years drinking), (2) diabetes-related data (number of complication, fasting insulin, HOMA-IR), (3) renal function (creatinine, uric acid), (4) circulatory dynamics (blood pressure, heart rate) and (5) questionnaire result (Physical Functioning in SF-36).
4. The multivariate analysis using a proportional odds model showed SAS severity (3% ODI) was related with age, sex, BMI, heart rate, creatinine and hypertension.

Discussion

1. As in the U.S.A. and Europe, SAS prevalence among Japanese diabetics is higher compared with general population (1.7%; Kayukawa *et al*. Biomedicine and Therapeutics, 1996).
2. The estimated SAS prevalence among diabetics with BMI < 25 suggests obesity is not the sole factor for SAS in diabetics.
3. ODI was correlated with number of diabetic complication, fasting insulin and HOMA-IR, suggesting a potential association between SAS and diabetic pathologies.
4. Lack of correlation between QOL questionnaire survey results and ODI shows diabetics are unaware of their symptoms even if they have concurrent SAS.
5. SAS affects blood glucose control in type 2 diabetics (Gottlieb *et al*. Arch Intern Med, 2005) and is an independent risk factor for cardiovascular disease (macrovascular disease) (Somers *et al*. Circulation, 2008).
6. Based on the results of this study, we propose to implement it actively screening for SAS in patients with diabetes.
7. The significant factors shown in the multivariate analysis, age, male, BMI, heart rate, hypertension and creatinine, are important determinants of candidate diabetics for SAS screening.
8. It remains uncertain relationship between diabetes and SAS, therefore we are planning the longitudinal study to reveal it for Japanese patients.