

Prevalence of Obesity and Risk of Obstructive Sleep Apnea among People with Type II Diabetes Mellitus

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Abstract

Background and Objective: Obesity is a major risk factor for the development of type 2 diabetes mellitus (T2DM) and obstructive sleep apnea (OSA). We aimed to assess the prevalence of obesity and risk of OSA among people with T2DM.

Materials and Methods: In a cross-sectional study, some basic, anthropometric, and physiological characteristics of 773 patients were assessed during their first visit to Diabetes Clinic of Sabzevar City, Iran. Risk of OSA was determined using the Berlin Questionnaire. Moreover, relationships among risk of OSA and basic, anthropometric, and physiological measures were evaluated using logistic regression modeling.

Results: Prevalence of overweight and obesity were 44.3% and 42.4%, respectively. Moreover, mean body mass index (BMI) (30.1 kg/m² vs. 27.8 kg/m²) and the rate of obesity (48.6% vs. 27.8%) were significantly higher in women than in men. The findings of Berlin Questionnaire showed that 73.6% of patients were at high risk for OSA. Patients aged 51 to 60 were at elevated risk for OSA [adjusted odds ratio (AOR) = 3.60, 95% confidence interval (CI) = 1.71-7.56]. Obese patients (AOR = 1.96, 95% CI = 1.11-3.46) and high systolic blood pressure (SBP) (AOR = 2.25, 95% CI = 1.47-3.44) showed significant association with OSA.

Conclusion: More than 85% of patients with T2DM were overweight or obese, and nearly three-quarter of them may be at higher risk for OSA. As weight loss, especially through exercise, seems to have beneficial effects not only on OSA severity, but also on consequences of T2DM, weight management should be highly recommended in this population.

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Introduction

Type 2 diabetes mellitus (T2DM), which is largely the result of excess body weight and lack of physical inactivity, is a progressive metabolic illness. It is a growing epidemic affecting more than 422 million people globally, and it is predicted to be the 7th leading cause of death in 2030 (1). Patients with T2DM usually have multiple comorbidities that make the disease management more complicated. Appropriate identification, evaluation, and treatment of these comorbidities

can lead to more effective disease management and, in turn, may improve patients function, quality of life, and mortality risk (2). Obesity, which refers to an excess amount of fat in the body, is one of the most prevalent comorbidities in people with T2DM. Although overweight and obesity are usually considered as a risk factor for T2DM, but it has been shown that diabetes, its concurrent conditions, consequences, and drugs used for disease management (e.g., insulin and sulfonylureas) may lead to weight gain as well, so they can aggravate the overweight and obesity in this population (3). Accordingly, Thomas et al. showed that in Australia 53 percent of patients with T2DM were obese and 32.8 percent were overweight (4). Al-Sharafi and Gunaid reported that the rates of

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overweight and obesity in people with T2DM in Yemen were 58.5 percent and 28.8 percent, respectively (5).

Sleep disorder is another common comorbidity in people with T2DM that deserves attention in the overall approach to the care of these patients (6). Obstructive sleep apnea (OSA) is the most common type of sleep disorder in this population. It is a chronic disorder characterized by periods of decreased breathing (hypopnea) or absence of breathing (apnea) during sleep, which is attributed to obstruction of upper airway (7). OSA and diabetes share common risk factors such as age and central obesity. Moreover, studies have shown that OSA and T2DM usually exist concurrently. There is also a bidirectional association between them, where OSA is highly prevalent among people with diabetes and on the other hand, the level of glycosylated hemoglobin (HbA1c) increases linearly with the severity of OSA (8, 9). Both OSA and obesity are common in people with T2DM and they increase the risks for stroke, heart failure, neuropathy, depression, road traffic accidents, cancer, and mortality (10). However, it is not known precisely that OSA in people with diabetes is due to the insulin resistance and diabetes itself or is secondary to overweight or obesity which usually exists in people with diabetes. Therefore, the primary aim of the present study was to assess the prevalence of overweight, obesity, and risk of OSA in adults with T2DM. The secondary aim was to investigate the association of body mass index (BMI) and some physiological measures involved in the risk of OSA in this population.

Materials and Methods

This was a cross-sectional study of patients with DM attending Diabetes Clinic of Sabzevar City, Iran. The study population consisted of 828 persons who attended the clinic since 2013 to 2015. After initial screening and excluding patients with type 1 diabetes and patients with missing data, 773 patients with T2DM aged 31-84 years were included in the study. Data of registered patients, including all routinely collected basic and clinical data, were extracted from their files. Extracted data were anonymized before analysis and included age, gender, education, medications, height, weight, neck circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP), duration of diabetes, and HbA1c. BMI was calculated using height and weight data

($BMI = w/h^2$; w = weight in kg, h = height in m). Overweight and obesity were defined according to World Health Organization (WHO) definitions: underweight: $BMI < 18.5 \text{ kg/m}^2$, normal weight: $BMI = 18.5\text{-}24.9 \text{ kg/m}^2$, overweight: $BMI = 25\text{-}29.9 \text{ kg/m}^2$, and obesity: $BMI \geq 30 \text{ kg/m}^2$ (10).

Moreover, Berlin Questionnaire was administered to evaluate the risk of OSA, which includes eleven items. These items cover three domains related to the risk of OSA, and subjects who scored ≥ 2 were considered as high risk, whereas subjects who scored < 2 were considered as low risk for OSA (6).

Finally, the collected data were analyzed using Stata software (version 12, Stata Corporation, College Station, TX, USA). Independent samples t-test was conducted to examine the differences between groups. Cross-sectional odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were estimated using logistic regression modeling. The level of statistical significance was set at $P \leq 0.05$.

Results

Women comprised 70.2% (mean age: 57.4 ± 9.6 years) and men comprised 29.8% (mean age: 60.6 ± 10.3 years) of subjects. Over 90 percent of patients (94%) were treated with two or more hypoglycemic medications and 21.5% of participants used insulin, either alone or in combination with other medications, and more than 16% of patients reported use of sleeping pills. Table 1 summarizes the baseline characteristics of the study population. Overall, comparison of baseline characteristics between men and women indicated that there were significant differences in age, BMI, neck circumference, duration of diabetes, and education but not in HbA1c, SBP, and DBP (Table 1).

The total prevalence of underweight, overweight, and obesity in men and women in different age groups are summarized in table 2. According to the results, the total prevalence of underweight, overweight, and obesity in women were 0.2%, 40.2%, and 48.6%, respectively; but in men they were 1.3%, 53.9%, and 27.8%, respectively. The prevalence of obesity was highest in patients aged 51-60 years among women (53.4%) and in patients aged 61-70 years among men (38.5%). Moreover, cumulatively, 88.8% of women and 81.7% of men were considered as either overweight or obese and just 11% of women and 17% of men were considered to have normal weight.

Table 1. Baseline characteristics and medical profile of the study population

Variable	Women (n = 543)	Men (n = 230)	Total (n = 773)	P-value
Age (year) [£]	57.4 ± 9.6	60.6 ± 10.3	58.4 ± 9.9	< 0.001
BMI (kg/m ²) [£]	30.1 ± 4.4	27.8 ± 3.8	29.4 ± 4.4	< 0.001
Neck circumference (cm) [£]	35.3 ± 2.3	39.9 ± 2.8	36.6 ± 3.3	< 0.001
HbA1c (%) [£]	8.8 ± 1.9	8.7 ± 1.6	8.8 ± 1.8	0.197
SBP (mmHg) [£]	133.4 ± 22.2	134.0 ± 20.6	133.6 ± 21.7	0.724
DBP (mmHg) [£]	76.5 ± 11.1	76.4 ± 10.6	76.5 ± 10.1	0.925
Duration of diabetes (year) [£]	8.2 ± 4.3	9.5 ± 5.3	8.6 ± 4.7	0.001
Education (% illiterate) ^F	44.5	22.6	38.0	< 0.001
Diabetic therapy (% ≥ 2 medications) ^F	95	92	94	-

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HbA1c: Hemoglobin A1c

* Significant level: $\alpha < 0.050$, [£] Data are presented in mean ± standard deviation (SD), ^F Data are presented in percent

In addition, 0.2% of women and 1.3% of men were considered as underweight (Table 2). There was also a significant difference between the mean BMIs for women and men in patients aged 41-50 (P = 0.004), 51-60 (P < 0.001), and > 71 (P = 0.016) years, but not in patients aged 30-40 (P = 0.641) and 61-70 years (P = 0.150). In underweight, normal, and overweight patients there was a male predominance, whereas in obese patients there was a female predominance (48.6% vs. 27.7%).

Table 2. Prevalence of underweight, normal weight, overweight, and obesity

Age groups (Number)	Under- weight	Normal weight	Overweight	Obese
Women				
31-40 (28)	0 (0)	39.3 (11)	35.7 (10)	25.0 (7)
41-50 (90)	0 (0)	5.6 (5)	45.4 (41)	49.0 (44)
51-60 (219)	0 (0)	9.1 (20)	37.5 (82)	53.4 (117)
61-70 (152)	0.7 (1)	10.5 (16)	40.1 (61)	48.7 (74)
> 71 (54)	0 (0)	18.5 (10)	46.3 (25)	35.2 (19)
Total (543)	0.2 (1)	11.0 (62)	40.2 (219)	48.6 (261)
Men				
31-40 (13)	0 (0)	15.4 (2)	76.9 (10)	7.7 (1)
41-50 (27)	0 (0)	18.5 (5)	48.2 (13)	33.3 (9)
51-60 (66)	1.5 (1)	24.3 (16)	51.5 (34)	22.7 (15)
61-70 (78)	0 (0)	12.8 (10)	48.7 (38)	38.5 (30)
> 71 (46)	4.3 (2)	15.3 (7)	60.8 (28)	19.6 (9)
Total (230)	1.3 (3)	17.0 (40)	53.9 (124)	27.8 (64)
Total (773)	0.5 (4)	12.8 (102)	44.3 (343)	42.4 (323)

Data are presented in % (n)

Based on the result of Berlin Questionnaire, in total, 73.6% of patients were classified as high risk, and 26.4% were classified as low risk for OSA. Moreover, compared with men, the odds of OSA was significantly higher in women (P = 0.004, 75.9% vs. 68.3%). Results also showed that except for age group of 31-40, in all age groups the odds of OSA was higher in women

than in men (Figure 1).

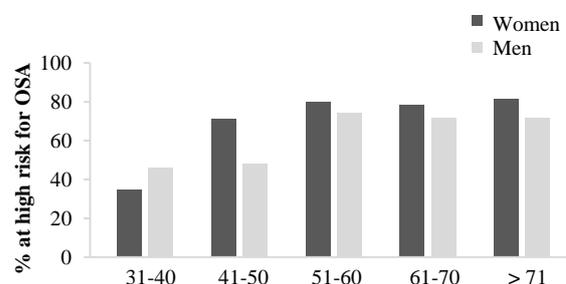


Figure 1. Proportion of patients at high risk of obstructive sleep apnea (OSA) in different age groups

In simple logistic regression analysis, we found significant relationship between OSA and BMI, gender, education, DBP, SBP, and age. After adjustment for potential confounding factors (in multiple logistic regression), compared to patients with normal weight, obese patients were at higher risk of developing the OSA (OR = 1.96, 95% CI = 1.11-3.46). Furthermore, SBP had higher odds for OSA (OR = 2.25, 95% CI = 1.47-3.44). Age group of 51-60 years was associated with an increased risk of OSA (OR = 3.60, 95% CI = 1.71-7.56) compared to age group of 31-40 years old. We could not find any association between OSA and gender, education, DBP, HbA1c, duration of diabetes, and neck circumference according to the model (Table 3).

Discussion

Our study aimed to investigate the prevalence of overweight, obesity, and risk of OSA among people with T2DM in Sabzevar City; moreover, we explored the associations between some basic and physiological measures and the risk of OSA among this population.

Table 3. Association of risk factors and OSA in people with type II diabetes mellitus (T2DM)

Variable	OR* (95% CI)	OR** (95% CI)	P-value (adjusted)
	-	0.10	0.010
BMI (kg/m ²)			
18.5-25	Ref	Ref	-
25-29	0.90 (0.56-1.44)	0.72 (0.43-1.19)	0.200
≥ 30	2.87 (1.72-4.80)	1.96 (1.11-3.46)	0.010
Gender			
Women	1.46 (1.04-2.05)	1.23 (0.80-1.91)	0.320
Education			
Illiterate	Ref	Ref	-
< Diploma	0.66 (0.46-0.95)	0.88 (0.58-1.34)	0.570
≥ Diploma	0.45 (0.28-0.71)	0.86 (0.49-1.50)	0.600
SBP (mmHg)			
Yes	3.17 (2.18-4.16)	2.25 (1.47-3.44)	< 0.001
DBP (mmHg)			
Yes	4.39 (1.33-14.43)	1.73 (0.49-6.07)	0.520
Age (year)			
31-40	Ref	Ref	-
41-50	3.00 (1.42-6.27)	2.36 (1.09-5.11)	0.020
51-60	5.73 (2.88-11.42)	3.60 (1.71-7.56)	0.001
61-70	4.97 (2.47-9.97)	2.17 (0.76-4.89)	0.050
> 71	5.23 (2.39-11.42)	1.81 (0.64-5.15)	0.250
Duration of diabetes	1.05 (1.01-1.09)	1.00 (0.94-1.05)	0.050
HbA1c	1.00 (0.91-1.09)	0.99 (0.90-1.09)	0.900
Neck circumference (cm)			
> 40	1.20 (0.74-1.94)	1.06 (0.98-1.15)	0.850

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HbA1c: Hemoglobin A1C;

OR: Odds ratio; CI: Confidence interval

* In unconditional logistic regression, we reported crude odds ratios (ORs).

** Calculated odds ratios (ORs) were adjusted for all variables in the table

Our results showed that 86.7% of patients had BMI ≥ 25 kg/m² (44.0% were overweight and 42.6% were obese), while the range of overweight and obesity prevalence in general population in Iran are estimated to be 27.0%-38.5% and 12.6%-25.9%, respectively (11). Thus, the finding of this study shows a considerably higher prevalence of obesity in patients with T2DM than in the general population. Our finding about higher prevalence of overweight and obesity in patients with T2DM was consistent with the findings of some previous studies. Al-Sharafi and Gunaid showed that 87.3% of patients with T2DM had BMI ≥ 25 kg/m² (5). Daousi et al. reported that 86% of patients with T2DM were overweight or obese (12). However, some other studies have indicated that the rate of overweight and obesity in patients with diabetes is considerably lower. Basukala et al. reported that rate of overweight and obesity in patients with diabetes was 51.9% (13). In addition, Pandeya et al. showed that 50% of the diabetics were overweight and obese (14). This considerable difference in rate of overweight and obesity in our study compared to those of Basukala et al. and Pandeya et al. may be due to differences in ethnicity, nutritional habits, physical

activity, and sociocultural issues.

Our results also indicated that mean BMI (30.1 kg/m² vs. 27.8 kg/m²) and the rate of obesity (48.6% vs. 27.8%) were significantly higher in women compared to men, and these differences persisted in almost all age groups. This result is consistent with the worldwide data showing that generally women have a higher mean BMI than men (15), and it is consistent with the findings of some previous studies about higher rate of obesity in diabetic women compared to men (5, 12, 13). Factors such as childbearing, hormonal status, and the high illiteracy rate, which lead to lower awareness about importance of physique, may be responsible for this difference. Additionally, some social and cultural practices limit physical activity and exercise in women, which could result in sedentariness, obesity, and related complications in them (13, 16). In our study, peak rate of obesity in women was observed in 51 to 60 years age group; however, in men it was among 61 to 70 years age group, and the highest rate of men-women difference in prevalence of obesity was observed in 31 to 40 years age group (7.7% vs. 25.0%), a difference of more than three times. This trend indicates that age of obesity and its peak occurs at a consid-

erably lower age (a decade) in women. As increased BMI is now a well-established independent risk factor for the development of T2DM (17), it seems necessary to provide the patients, especially women, with more health education about obesity, diabetes, and the risk factors associated with the development of these health conditions.

Using the Berlin Questionnaire to classify the risk of OSA, we found that 73.6% of patients with T2DM were at high risk for OSA. In a recent study in general population, using the Berlin Questionnaire, Silva et al. reported that 42.4% of study population were at high risk for OSA (18). Grover et al. found relatively lower rate for risk of OSA (33%) using the Berlin Questionnaire in a sample of patients undergoing preventive examinations (19). In a multinational study using the Berlin Questionnaire, Netzer et al. reported that 35.8% of the study population was at high risk for OSA (20). These results indicate that in comparison to general population considerably greater proportion of patients with diabetes are at high risk for OSA. However, considerably different from our finding, Cass et al. reported that 48.6% of patients with diabetes were at high risk for OSA (6). In another study by Rabie et al., it has been found that 38% of patients with T2DM were at high risk for OSA (9). The finding of current study about risk of OSA in patients with diabetes is similar to the finding of Rabie et al. (9) and Cass et al. (6) in general population. OSA is a common and multifactorial disorder and its risk factors include advanced age, male gender, large neck circumference, hypertension, and BMI (21). So, it is difficult to justify the reasons of this inconsistent finding; however, a very important determinant factor in the risk of OSA and its severity is probably the BMI, and due to the fact that mean BMI of our study population was considerably higher than those of Cass et al. (6) and Rabie et al. (9), it may explain the observed inconsistency.

In addition, except for 31 to 40 years age group, in all age groups risk for OSA was considerably higher in women than in men. This finding is in contrast with the finding of studies which show that men are two to three times more likely to have OSA compared to women (22, 23). On the other hand, Cass et al. found no difference in the risk of OSA in men and women (6). Mean BMI for women in our study was considerably higher than men (30.1 kg/m² vs. 27.8 kg/m²). As a result, a greater proportion of women met the BMI crite-

ria for OSA risk than did men. So, the greater prevalence of obesity in women may explain partially the higher rate of OSA risk observed in present study. Moreover, there was an increased risk of OSA with advancing age. The risk of OSA peaked at around age 60 and started to decline thereafter, especially in men. This finding is similar to the distribution of risk observed in a previous study by Cass et al. (6). However, in women the peak rate was observed in age group of > 71, which is similar to the findings of some epidemiologic studies that reported an increase in sleep-disordered breathing (SDB) and OSA with advancing age (7, 23, 24).

Additionally, in multiple logistic regression model, high SBP was predictive of risk for OSA in women, but not in men. Epidemiologic data support that there is a bidirectional association between OSA and hypertension, and the strength of this relationship seems to be modulated by factors such as age and gender (25). Perhaps the Wisconsin Sleep Cohort Study (WSCS) provided the most convincing prospective data in support of the relationship between OSA and hypertension. The findings of that study indicated an independent dose-response relation between SDB and hypertension (26). However, more studies are needed to identify the possible mechanisms that link the OSA and hypertension in people with T2DM. Finally, although the population of this study included a wide age range, more than half of the participants were women, and we collected clinically-important data, there were also some limitations. As with all cross-sectional studies, cause and effect relationships must be interpreted with caution. Moreover, we used Berlin Questionnaire to assess the risk of OSA, and we were not able to confirm OSA with a formal sleep study.

Conclusion

In summary, findings of this study indicate a considerably high prevalence of overweight and obesity in individuals with T2DM; moreover, the results show that great proportion of these patients are at high risk for OSA and it appears that obesity is the link between T2DM and OSA. Considering the fact that intermittent hypoxia, which is common in OSA, can decrease insulin sensitivity and increase sympathetic activity and proinflammatory cytokines (27), this finding provide scientific-based evidence about the importance of OSA management in patients with diabetes. Moreover,

due to the strong relationship between obesity and hypertension and the causal role of OSA in precipitating and perpetuating hypertension (28), these findings which show high prevalence of obesity and higher risk of OSA in patients with diabetes, have considerable importance for clinicians and health care providers. Finally, as weight loss, especially through exercise, seems to have beneficial effects not only on OSA severity, but also on cardiometabolic consequences of OSA, obesity, and diabetes (29), weight management should be highly recommended in this population, particularly in patients aged 51 to 60 years which are at higher risk for OSA than other age groups.

Conflict of Interests

Authors have no conflict of interests.

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