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The prevalence of high risk obstructive sleep apnoea among patients with type 2 diabetes in Jordan

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ABSTRACT

Objective: To estimate the prevalence of Obstructive Sleep Apnea (OSA) among patients with type 2 Diabetes Mellitus (T2DM) in Jordan, and to explore the association between sleep apnea and clinical and demographic variables.

Method: A cross-sectional study was carried out from the 1st of November 2011 to the 1st of February 2012 on 1143 patients with T2DM (aged 30–90 years) at the National Center for Diabetes, Endocrinology, and Genetics (NCDEG). The center is considered to be the only referral center in the country and accordingly, the patients represent the population in different parts of the country. All participants completed the Arabic version of the Berlin Questionnaire and were categorized as either low or high-risk patients for OSA.

Results: A total of 1143 patients with T2DM were included in this study. There were 587 (51.4%) males and 556 (48.6%) females. The findings showed that 554 (48.5%) patients were at high risk for OSA and 589 (51.5%) were low risk for OSA. Logistic regression analysis revealed that age, smoking, and neck circumference were significantly correlated with high risk for OSA. The clinical and demographic variables were also collected for analysis.

Conclusions: The study found that high risk for OSA was highly prevalent among Jordanian patients with T2DM and that age, smoking and neck circumference were significantly correlated with OSA. Health care providers should be made aware of the high prevalence of sleep problems affecting patients with diabetes and should consider the appropriate screening and treatment for these patients, therefore improving their quality of life.

1. Introduction

Obstructive Sleep Apnea (OSA); is a common disorder; affecting approximately 3%–7% of adult men and 2%–5% of adult women in the general population [1]; and is being increasingly recognized as an important cause of morbidity and mortality [2]. The National foundation indicates that one in four adults and about 57% of patients with obesity are at high risk for OSA [3]. This clinical condition is characterized by repeated episodes of complete or partial obstruction of the upper airway during sleep time, associated with increased respiratory efforts, intermittent arterial oxygen desaturation and sleep fragmentation [4]. It is now well established that OSA is associated with an increased risk for cardiovascular

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diseases, cerebrovascular diseases, congestive heart failure, and this is related to the pathophysiological changes of OSA including intermittent hypoxia, sleep fragmentation, increase sympathetic activity and deoxygenated phenomena [4].

Diabetes is also associated with a higher incidence of cardiovascular, cerebrovascular, and renal disease [5,6]. T2DM is increasingly common worldwide reaching epidemic proportion [7]. It is estimated that the world prevalence of diabetes mellitus (DM) among adults will increase to 7.7% and 439 million adults by 2030, between 2010 and 2030 there will be a 69% increase in the number of adults with diabetes in developing countries and a 20% increase in developed countries [8]. In Jordan, the age-standardized prevalence of DM and impaired fasting glucose (IFG) were 17.1% and 7.8% respectively, which emphasize that the prevalence was high in Jordan and is yet increasing [9]. Patients with diabetes typically associated with cardiovascular disease similar to OSA and it is important to study the relationship between these two conditions.

OSA and T2DM commonly coexist, where several cross-sectional studies showed a high prevalence of OSA among patients with T2DM and a high prevalence of T2DM among patients with OSA [52,53]. OSA is associated with worse glycemic control and is considered an important risk factor for glucose dys-metabolism. Several studies have demonstrated that OSA is associated with increased insulin resistance and glucose intolerance independent of obesity [10–14]. OSA could lead to the development or progression of micro and macro vascular complications in patients with T2DM, although evidence of favorable impact of OSA treatment on these outcomes remains largely lacking.

T2DM is a major public health concern with high mortality, morbidity, and health-care costs with the prevalence of T2DM being high in the Jordanian population [24–26]. Chronic sleep fragmentation, sleep deprivation and intermittent nocturnal hypoxemia associated with OSA have been implicated in metabolic dysfunction, including altered glucose metabolism and adverse cardiovascular complications [12,27]. Multiple studies in the literature have shown a high prevalence of OSA among T2DM patients, and as such, the aim of this study is to estimate the prevalence of high risk OSA among patients with T2DM and to explore if sleep apnea is associated with clinical and demographic variables.

2. Methods

2.1. *Study design and settings*

We conducted a cross-sectional study from the 1st of November 2011 to the 1st of February 2012 on 1143 patients with T2DM (30–90 years) at the National Center for Diabetes, Endocrinology, and Genetics (NCDEG) in Amman, Jordan. The center is considered to be the only referral center in the country and accordingly, the patients attending the center represent the population in different parts of the country. All participants completed the Berlin Questionnaire and were categorized as either low or high-risk patients for OSA. We also collected the data on patients 'gender, age, level of education, DM duration, smoking status and type of DM treatment. The data was collected after taking verbal approval from the patients with diabetes to participate in the study and after they had signed the consent form.

2.2. *Inclusion criteria*

Participants aged between 30 and 90 years old, diagnosed with T2DM according to the American Diabetes Association (ADA) and were attending the general outpatient clinic's every 1–3 months as part of their routine follow up were included in the study.

2.3. *Exclusion criteria*

Patients with type 1 diabetes and pregnant or breastfeeding women were excluded from this study.

2.4. *Ethical approval*

The study was approved by the Research and Ethical Committee of NCDEG in Amman, Jordan. The participation of the patients with diabetes was voluntary and the data collected during the study was handled with confidentiality.

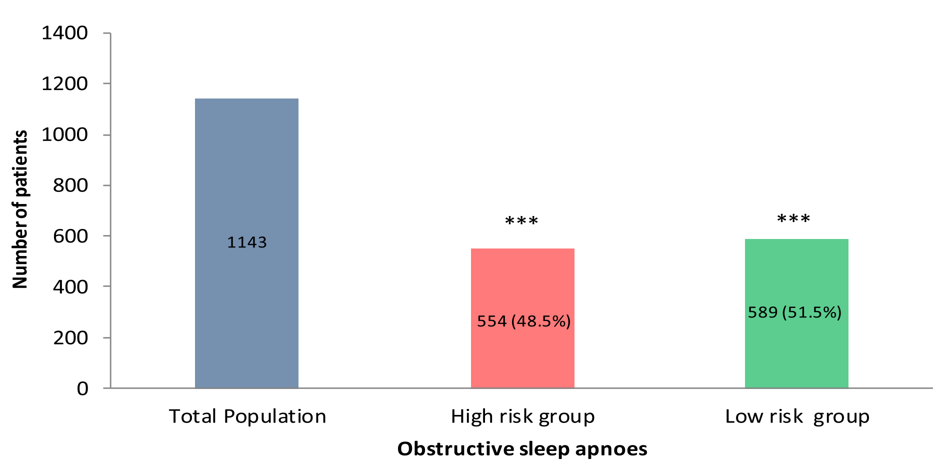

Fig. 1 – The prevalance of Obstructive sleep apnoea syndrome among the type 2 diabetes patients.

3. Measures

3.1. Anthropometric measurements

Height was measured without shoes, to the nearest 0.5 cm using a stadiometer with shoulders in a relaxed position and the arms hanging freely. Weight was taken with the patient wearing light clothes and without shoes and was measured to the nearest 0.5 kg. Body Mass Index (BMI) was obtained by dividing the weight in kilograms by the square of height in meters [15]. By using non-stretchable tapes, waist circumference was measured to the nearest centimeter. The measuring tape was put at the level midway between the iliac crest and the lower rib margin in a horizontal scale, also (Waist/Height) ratio was obtained by dividing the waist in cm on height in cm. Neck circumference (NC) was measured to the nearest 0.5 cm using a non-stretchable tape around the neck just below the most prominent portion of the thyroid cartilage, the laryngeal prominence (Adam's apple) [16].

3.2. Clinical and laboratory measurements

Glycosylated hemoglobin (HbA1c) was tested by using a high-performance liquid chromatography method (Bio-Rad) [17] and the last result was computed. Moreover, information about medical history; the presence of hypertension, dyslipidemia, coronary artery disease erectile dysfunction and the type of treatment (i.e. oral hypoglycemic agents, insulin or both hypoglycemic agents and insulin) were collected from the medical records at the time of interview.

3.3. Structured questionnaire

The Arabic version of the Berlin Questionnaire (ABQ) was used to assess the symptoms and risk of OSA [18]. The ABQ questionnaire includes 10 items five items on snoring (category 1, items 1–5), three items on daytime somnolence (category 2, items 6–8), and two items on the history of hypertension and/or body mass index (BMI) > 30 kg/m^2 (category 3, items 9, 10). The ABQ was scored as previously reported by Netzer et al [19]. The snoring or daytime somnolence categories are positive if responses indicate persistent symptoms (>three to four times a week) on the questionnaire items. A positive score on the third category requires a history of hypertension or a BMI of greater than 30 kg/m^2. Study patients were classified as being at a high risk of having sleep apnea if scores were positive on two or more of the three categories. Those patients who scored positively on less than two categories were identified as being at a low risk of having sleep apnea. Translation and construct validity and reliability of the Arabic version of Berlin questionnaire using alpha Cronbach test was performed and the results was 0.92 for the 10 items of ABQ [18].

3.4. Waist and neck circumference

Waist and neck circumference was considered normal in women if it was less than 88 cm, and in men, if it was less than 102 cm according to ATP III criteria [20]. Neck circumference was considered normal if it was ≤43 cm for men and ≤38 cm for women [21].

3.5. Glycosylated hemoglobin (HbA1c)

HbA1c was stratified into three groups: good glycemic control if HbA1c < 7%, fairly controlled if HbA1c 7 – 8.5% and poor glycemic control if HbA1c > 8.5%.

3.6. Dyslipidemia

According to ADA criteria 2011 [22], lipid levels were considered abnormal if HDL level ≤ 40 mg/dl in men and ≤50 mg/dl in women, LDL level ≥ 100 mg/dl and triglyceride ≥ 150 mg/dl.

Table 1 – Socio-demographic, clinical and laboratory characteristics of study participants.

Variable		N	%
Sex	*Male*	587	51.4
	Female	556	48.6
Age (years)	<40	36	3.2
	40–59	559	48.9
	≥60	548	47.9
Level of education	*<high school*	343	30.0
	=high school	192	16.8
	>high school	608	53.2
Smoking	*Nonsmoker*	725	63.4
	Ex-smoker	190	16.6
	Smoker	228	20
Duration of diabetes (years)	<5	378	33.1
	5–9	262	22.9
	>10	503	44
Body mass index (kg\m^2)	<25	90	7.8
	25–29.9	370	32.4
	≥30	683	59.8
Waist circumference (cm)	*Normal*	301	26.3
	For men < 102		
	For women < 88		
	Abnormal	842	73.7
	For men > 102		
	For women ≥ 88		
Neck circumference (cm)	*Normal*	829	72.5
	For men ≤ 43		
	For women ≤ 38		
	Elevated	314	27.5
	For men > 43		
	For women > 38		
Hypertension	Yes	860	75.2
	No	283	24.8
Dyslipidemia	Yes	929	81.3
	No	214	18.7
HbA1c (%)	<7	355	31.0
	7–8.5	505	44.2
	>8.5	283	24.8

3.7. Hypertension

Hypertension was considered if diastolic blood pressure ≥ 80 mmHg or systolic blood pressure ≥ 130 mmHg. Also, patients were considered as hypertensive if they were on anti-hypertensive therapy at the time of attending the diabetic clinic at the NCDEG [22].

3.8. Smoking status

According to the world health organization (WHO) guidelines, the smokers were classified into three groups; Past smoker (Ex-smoker): a person who was previously occasionally or a daily smoker, but currently did not smoke at all. Current smoker: a person who smoked cigarettes occasionally or daily. Nonsmoker: a person who has smoked very little in the past or has never smoked before [23].

3.9. Statistical analysis

Statistical analysis was performed using Statistical Package for Social Science (SPSS, version 16). First, the data were tested for data entry errors and outlying values. Descriptive statistics were obtained, such as the mean value and standard deviation for continuous variables and frequency distribution for categorical variables.

The prevalence of high risk for OSA was expressed as a percentage. A bivariate relationship between HR-OSA and a number of independent variables were examined for statistical significance using chi-square analysis. A p-value < 0.05 was considered statistically significant. Multivariate logistic regression was used to examine the net effect for each of the independent variables on a dependent variable.

4. Results

The mean age of the patients was 58.6 ± 10 years. Out of 1143 patients, 587 were (51.4%) males and 556 (48.6%) were females (age range between 30 and 90 years). The findings showed that 554 (48.5%) patients were at high risk for OSA and 589 (51.5%) were low risk for OSA (see Fig. 1). The socio-demographic and clinical characteristics are presented in Table 1. The comparisons of high-risk OSA and low risk of OSA on socio-demographic and clinical parameters are shown in Table 2. The analysis showed that there was no significant correlation between high-risk OSA and low-risk OSA on the patients' gender, age, level of education, smoking status, duration of diabetes, dyslipidemia or HbA1c level. However, a significant difference was found between high-risk OSA and low-risk OSA on neck circumference (P < 0.0001).

Socio-demographic, laboratory and clinical factors affecting high risk for obstructive sleep apnea are presented in Table 3. The results showed the patients who aged ≥40 years were at high risk for OSA. Patients who aged between 40 and 59 years were 2.26 times more likely to have had a high risk for OSA than those who aged less than 40 years, and people who aged ≥ 60 years were 2.3 times more likely to have had a high risk for OSA than those less than 40 years of age.

The current smoker was 1.45 times more likely to have high risk for OSA than patients who never smoked and this

Table 2 – Prevalence of high and low risk for OSA in study population according to the socio-demographic, clinical and laboratory characteristics.

Variable		HR-OSA* [n (%)]	LR-OSA** [n (%)]	P-value¥
Sex	Male	273(49.3%)	314(53.3%)	0.173
	Female	281(50.7%)	275(46.7%)	
Age (years)	<40	12(2.2%)	24(4.1%)	0.178
	40–59	272(49.1%)	287(48.7%)	
	≥60	270(48.7%)	278(47.2%)	
Level of education	<high school	180(32.5%)	163(27.7%)	0.101
	=high school	97(17.5%)	95(16.1%)	
	>high school	277(50.0%)	331(56.2%)	
Smoking	Nonsmoker	338(61.0%)	387(65.7%)	0.254
	Ex-smoker	99(17.9%)	91(15.4%)	
	Smoker	117(21.1%)	111(18.8%)	
Duration of Diabetes	<5	183(33.0%)	195(33.1%)	0.753
	5–9	132(23.8%)	130(22.1%)	
	≥10	239(43.1%)	264(44.8%)	
Neck circumference (cm)	Normal	347 (62.6%)	482 (81.8%)	0.000
	Elevated	207 (37.4%)	107 (18.2%)	
Dyslipidemia	Yes	462(83.4%)	467(79.3%)	0.075
	No	92(16.6%)	122(20.7%)	
HbA1c (%)	<7	167(30.1%)	188(31.9%)	0.614
	7–8.5	243(43.9%)	262(44.5%)	
	>8.5	144(26.0%)	139(23.6%)	

* **HR-OSA**: high risks of obstructive sleep apnoea.
** **LR-OSA**: low risks of obstructive sleep apnoea.
¥ P-value < 0.05 considered statistically significant.

Table 3 – Logistic regression analysis for socio-demographic, laboratory and clinical factors affecting high for obstructive sleep apnea.

Variable	OR	P-value*
Smoking		
Nonsmoker	1	
Ex-smoker	1.348	0.100
Current smoker	1.454	0.025
Neck circumference		
Normal	1	
Elevated	2.75	0.000
Age groups		
<40	1	
40–59	2.257	0.03
≥60	2.318	0.03
Sex		
Male	1	
Female	1.0	0.980
HbA1c		
<7	1	
7–8.5	1.010	0.947
>8.5	1.001	0.995
Duration of DM		
<5	1	
5–9	0.906	0.568
≥10	0.815	0.202
Dyslipidemia		
No	1	
Yes	1.200	0.256
Level of education		
<high school	1	
=high school	0.920	0.662
>high school	0.810	0.184

* P-value < 0.05 considered statistically significant.

association was statistically significant (P < 0.025). Those who had elevated neck circumference were found to be 2.8 times more likely to have high risk for OSA than those with normal neck circumference (P < 0.0001).

5. Discussion

OSA has been identified as a highly prevalent comorbidity of type 2 diabetes and in particular among obese patients with type 2 diabetes [28–30]. The prevalence of OSA is on the rise due to a worldwide surge in the aging of populations and obesity [31]. In this study, we found that high risk for OSA is highly prevalent (48.5%) in the patients with diabetes and this was in agreement with previous studies [32–34]. A recent study from the United States also found that sleep problems are highly prevalent, with 10% to 40% reporting any given problem and>90% of patients reported any examined sleep problem [35]. Shim et al. also found that patients with T2DM using the Berlin Questionnaire showed higher (50.8%) risk of OSA [36]. We reported a higher prevalence rate of high risk for OSA as compared to what was found by Shim et al.'s study. This could be explained by the fact that about 48% of our study sample population were above the age of sixty. Age alone is a risk factor for sleep apnea, add to diabetes chronic illness associated with other comorbidities (hypertension and obesity), both diseases have been associated with obstructive sleep apnea. The results of this study were also close to what had been reported by West, et al. [37] who sought to assess the prevalence of obstructive sleep apnea in men with type2 diabetes, in which they found the prevalence of HR-OSA to be 56%.

Many studies reported that the majority of patients with OSA are patients with obesity and demonstrated a range of comorbidities such as depression, diabetes, and hypertension. Hence, management, of OSA needs to be based on a holistic and multidisciplinary approach which includes lifestyle alteration [31,38,39]. Multiple studies have attempted to address the reason for age-related impact on OSA. Mechanisms suggested that for the increased prevalence of OSA in the elderly, reasons include changes in body structures surrounding the pharynx, lengthening of the soft palate and increased deposition of fat in the para pharyngeal area [40,41]. In our study, we found that OSA risk significantly increased with age. Due to the sequence of weight gain after middle age, upper respiratory tract becomes narrower, and it worsens obstructive sleep apnea syndrome (OSAS). Since mastication is in order to provoke and maintain arousal, patients with OSAS, who especially feel strong sleepiness, tend to lean towards obesity by frequent mastication which leads them to the tendency to overeat [42].

Many studies have reported that OSA is linked with higher HbA1c levels in patients with and without diabetes. The severity of hypoxemia in patients with OSA correlates with HbA1C levels ranging from normal to pre-diabetes and diabetes [43]. In contrast to this, our study found that there were no significant results between normal to pre-diabetes and diabetes.

Some studies concluded that male sex is a predictor risk factor for high risk OSA [44], and this is due to elevated mass in the neck and torso [45], but on the other hand, other studies found no significant relation between gender and High Risk for OSA [46]. In our study we were unable to demonstrate such a relation. A study done in Turkey used polysomnography test to assess sexes differences among patients with OSA found no significant differences between genders and this is similar to our findings [47].

Cigarette smoking has been shown to be a risk factor for high risk for OSA. Smoking is associated with a higher prevalence of sleep-disordered breathing and snoring [48,49]. A recent study reported that current smokers are at higher risk for sleep-disordered breathing than are never cigarette smokers. Heavy smokers have the higher risk while ex-smokers are not at greater risk for sleep-disordered breathing [50]. In the present study, current smokers were more likely to have High risk for OSA as compared to nonsmokers. This can be explained by the cigarette-induced damage and airway inflammation, which could increase the risk of collapsibility during sleep, as well as change the functional and structural properties of the upper airway [51].

The major limitation of this study is its cross-sectional nature as well as the limited number of risk factors examined exclusively to this center. Moreover, no actual OSA test was performed for the participants to diagnose OSA. Future research is needed to address these limitations.

In conclusion, this study found that high risk for OSA was highly prevalent among Jordanian patients with type 2 diabetes and age, smoking and neck circumference were significantly correlated with a high risk for OSA. Our findings suggest that more attention must be shifted towards Jordanian patients with diabetes and healthcare providers should be aware of the high prevalence of sleep problems affecting these patients in Jordan. Healthcare practitioners should consider the appropriate screening and treatment, which may improve patients' quality of life and in turn, prevent or minimize complications of diabetes mellitus, including OSA.

Declaration of Competing Interest

The authors declare no conflicting interests.

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