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Clinical Characteristics of Type 2 Diabetics Who are at High Risk for Obstructive Sleep Apnea

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) has been associated with insulin resistance and glucose intolerance. Recent reports have indicated that the majority of patients with type 2 diabetes (T2D) are also having OSA. **Aim/Objective:** The primary goal of the study is to assess the risk of OSA among T2D patients and its impact on T2D related control and complications. **Method:** A cross-sectional study for the adult patients with T2D who had a routine follow up visit from Jun 2013- Aug 2014 was asked to participate. We excluded patients with existed psychiatric illness and those with history of diagnosed OSA. To screen for OSA we used Berlin Questionnaire. **Result:** A total of 265 T2D patients were included in the study with a mean age of 57.2±12.5 years and long standing T2D. Around 53.2% were classified as high risk for OSA. Compared to those who are considered low risk for OSA, those who are high risk for OSA have higher BMI (p <0.001), higher mean SBP (p 0.002), less likely to be male (p 0.003), more likely to have hyperlipidemia (p 0.058), more likely have neuropathy (p 0.021), more likely to report sedentary lifestyle (p 0.046), and more likely to report low income (p 0.068). **Conclusion:** High risk T2D patients for OSA tend to be older, have significantly higher BMI, systolic BP and tend to have significantly higher risk for neuropathy.

Keywords: Sleep apnea, OSA, diabetes, T2D, Berlin.

1. INTRODUCTION

Diabetes is a growing health problem locally and globally. According to the recent International Diabetes Federation (IDF), 387 million people living with diabetes globally with an approximate 46.3% of them are been undiagnosed (1). This number expected to increase by the year of 2035 by 55% with the Middle East been 2nd region with the highest expected increase worldwide (2). The direct medical cost for diabetes management in USA has been estimated to be around 20%, which created overwhelming financial burden on health system (3).

Obstructive sleep apnea (OSA) is characterized by repetitive upper airway obstructions leading to intermittent hypoxia and sleep fragmentation. Recent study estimated the prevalence of OSA to be 20-30% in men and 10-15% in women (4, 5). The overnight polysomnography is considered to be the first line diagnostic study to diagnose OSA using the metric of hypopnea-apnea index (AHI) (4). AHI of > 5 events/hr are diagnostic for mild OSA, while AHI

> 15 events /hr are considered to be moderate-sever OSA (6).

Berlin questioner could be used to screen at risk patients for OSA diagnosis and the result stratified patients to high or low risk for OSA (7). A high risk score according to the Berlin questionnaire is associated with a sensitivity and specificity of 80% and 46% when OSA is defined as an AHI ≥ 5, and 91% and 37% when OSA is defined as an AHI ≥15 (7).

2. AIM

The primary goal of the study is to assess the risk of OSA among our type 2 diabetes (T2D) patients using a validated Berlin questionnaire as we lacked for a sleep lab at our center. Also we will evaluate the prevalence and the clinical characteristics of participants with high risk for sleep apnea and its relation to the measured cardiovascular markers.

3. MATERIAL AND METHODS

A cross-sectional study for patients with T2D at the King Abdulaziz Specialist Hospital, Taif, Saudi Arabia. T2D aged 18 years and older who had a routine follow up visit to the

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Diabetes clinic from Jun 2013- Aug 2014 were asked to participate and verbal consent was taken from the participants. We excluded patients with existed psychiatric illness and those with history of diagnosed obstructive sleep apnea.

Researchers interviewed the patients and collected the personal information. Vital signs, height and weight were measured in the same visit and Body Mass Index (BMI) was calculated. Recent laboratory data was collected from the patient's electronic medical record. Those who reports monthly income < 1335 USD were considered to have low income while those reports monthly income ≥4000 USD were considered to have high income. Data about physical activities, T2D related complications and medications were collected by the investigators.

To screen OSA risk we used Berlin Questionnaire. The questionnaire consists of 3 main categories related to the risk of having sleep apnea. Participants can be classified into high Risk or low Risk based on their responses to the individual items and their overall scores in the categories. The questionnaire is divided into 3 categories that evaluate sleeping/snoring habits, daytime sleepiness, and presence of hypertension (HTN)/ obesity. Patients was considered to have positive response in category 1 and/or 2 if they scored positive in ≥2 section in each categories. Those with BMI > 30 or has HTN considered to have positive response in category 3. Those who have positive response in 2 or more categories were considered high risk for sleep apnea or otherwise considered low risk for sleep apnea.

Data was collected in an Excel sheet and analyzed using the *Statistical Package for the Social Sciences* (SPSS) software V20. The Chi squared test was used to study the relationship between variables and the T-test was used to compare between means.

4. RESULTS

A total of 265 T2D patients were included in the study with a mean age of 57.2±12.5 years, long standing T2D, most of the included T2D patients have hypertension and hyperlipidemia, were obese, were married, did reports low income, and mostly with low level of education (Table 1). Metformin was the most commonly prescribed oral medication and 1/3 were on insulin. Majorities of the patients were on statin and aspirin. The most common complication was neuropathy and sever hypoglycemia. Most of the patients' reports sedentary lifestyle and few of them were active smokers.

Around 53.2% were classified as high risk for OSA (Table 2). Compared to those who are considered low risk for OSA, those who are high risk for OSA were older (p 0.470), have higher BMI (p <0.001), higher mean SBP (p 0.002), less likely to be male (p 0.003), have long T2D duration (p 0.238), more likely to have hypertension (p 0.013) and hyperlipidemia (p 0.058), and more likely to report low income (p 0.068).

Also those who are high risk for OSA were more likely to be on statin (p 0.007) but otherwise no difference in management.

| Baseline characteristics (N= 265) | |
|---------------------------------------|------------|
| Mean age (yrs) | 57.2±12.5 |
| Male (%) | 47.5 |
| Mean diabetes duration (years) | 11.3±8.6 |
| Hypertension (%) | 61.1 |
| Hyperlipidemia (%) | 69.4 |
| Mean BMI (Kg/m ²) | 32.0±6.5 |
| Mean systolic blood pressure (mmHg) | 141.2±23.6 |
| Mean diastolic blood pressure (mmHg) | 81.0±13.2 |
| Mean heart rate (beat per minute-bpm) | 81.6±13.4 |
| Socioeconomic | |
| Married (%) | 87.9 |
| Bachelor degree or higher (%) | 17.7 |
| Low income (%) | 66.4 |
| Medications | |
| Metformin (%) | 64.9 |
| Sulfonylurea (%) | 26 |
| DPP-4 inhibitors (%) | 9.1 |
| Insulin (%) | 30.2 |
| Statin (%) | 70.2 |
| ACE inhibitors/ ARB (%) | 50.1 |
| Aspirin (%) | 55.5 |
| Laboratory data | |
| HbA1c (%) | 8.6±1.8 |
| Total cholesterol (mg/dl) | 171.4±41.1 |
| LDL (mg/dl) | 101.5±38.5 |
| HDL (mg/dl) | 42.7±15.6 |
| Triglyceride (mg/dl) | 152.5±80.9 |
| Diabetes related complication | |
| End-stage renal disease (%) | 2.3 |
| Neuropathy (%) | 65.3 |
| Retinopathy (%) | 25.3 |
| Ischemic heart disease (%) | 27.5 |
| Cerebrovascular accident (%) | 10.9 |
| Sever hypoglycemia (%) | 28.3 |
| Lifestyle habits | |
| Sedentary lifestyle (%) | 75.8 |
| Active smoking (%) | 8.3 |

Table 1. Baseline characteristics for the whole cohort.

Regarding the complications those who were high risk for OSA were more likely have neuropathy (p 0.021) and non-statically significant higher risk of all complications except for ischemic heart disease which was more common in those who were considered low risk for OSA.

Regarding the lifestyle habits, those who were high risk for OSA were more likely to report sedentary lifestyle (p 0.046) and be active smoker (p 0.693).

5. DISCUSSION

Obesity is a growing health problem worldwide and the rates of obesity have tripled in developing countries (12). Obesity considered as a shared major risk factor for both OSA and T2D. Our study showed that T2D patients who were considered to have high risk for OSA were more likely to be obese. Adult with BMI of ≥40 was associated with a higher odd for diabetes (OR 7.37) (11). More recent retrospective study of more than 16000

| | High risk for OSA | Low risk for OSA | P value |
|---------------------------------------|-------------------|------------------|---------|
| Baseline characteristic | | | |
| Number of patients (%) | 141(53.2) | 124(46.8) | n/a |
| Mean age (yrs) | 57.7±11.9 | 56.6±13.1 | 0.470 |
| Male (%) | 39 | 57.3 | 0.003 |
| Mean diabetes duration (years) | 11.9±8.8 | 10.6±8.4 | 0.238 |
| Hypertension (%) | 68.1 | 53.2 | 0.013 |
| Hyperlipidemia (%) | 74.5 | 63.7 | 0.058 |
| Mean BMI (Kg/m ²) | 33.9±6.1 | 29.9±6.2 | <0.001 |
| Mean systolic blood pressure (mmHg) | 145.4±24.7 | 136.3±21.4 | 0.002 |
| Mean diastolic blood pressure (mmHg) | 82.0±14.2 | 79.8±11.8 | 0.159 |
| Mean heart rate (beat per minute-bpm) | 83.7±14.0 | 79.2±12.3 | 0.006 |
| Socioeconomic | | | |
| Married (%) | 84.4 | 91.9 | 0.156 |
| Bachelor degree or higher (%) | 15.6 | 20.2 | 0.593 |
| Low income (%) | 70.2 | 62.1 | 0.068 |
| Medications | | | |
| Metformin (%) | 61.7 | 68.5 | 0.244 |
| Sulfonylurea (%) | 24.8 | 27.4 | 0.631 |
| DPP-4 inhibitors (%) | 7.8 | 10.5 | 0.448 |
| Insulin (%) | 31.2 | 29.0 | 0.203 |
| Statin (%) | 77.3 | 62.1 | 0.007 |
| ACE inhibitors/ ARB (%) | 54.6 | 46.8 | 0.203 |
| Aspirin (%) | 56.0 | 54.8 | 0.846 |
| Laboratory data | | | |
| HbA1c (%) | 8.5±1.8 | 8.7±1.8 | 0.448 |
| Total cholesterol (mmol/L) | 173.2±44.0 | 169.3±37.5 | 0.506 |
| LDL (mmol/L) | 102.6±40.8 | 100.3±35.8 | 0.682 |
| HDL (mmol/L) | 43.86±17.2 | 41.4±13.7 | 0.285 |
| Triglyceride (mmol/L) | 156.3±86.3 | 148.1±74.5 | 0.485 |
| Diabetes related complication | | | |
| End-stage renal disease (%) | 3.5 | 0.8 | 0.135 |
| Neuropathy (%) | 71.6 | 58.1 | 0.021 |
| Retinopathy (%) | 28.4 | 21.8 | 0.218 |
| Ischemic heart disease (%) | 26.2 | 29.0 | 0.612 |
| Cerebrovascular accident (%) | 12.1 | 9.7 | 0.536 |
| Sever hypoglycemia (%) | 29.8 | 26.6 | 0.567 |
| Lifestyle habits | | | |
| Sedentary lifestyle (%) | 82.3 | 68.5 | 0.046 |
| Active smoking (%) | 8.5 | 8.1 | 0.693 |

Table 2. Baseline characteristics based on OSA risk stratification.

T2D patients showed that 18% of those have OSA and this figures increased to 23% with BMI of ≥ 30 (14).

In our study those who were high risk for OSA were significantly more likely to be female and non-significantly more likely to be older. A population-based study of men who underwent polysomnography, moderate-severe OSA was present in 63% of obese men compared to 11% and 21% of those who were normal weight and overweight respectively (9).. This was less pronounced for women as 22% of obese women had OSA compared to 3% and 9% of those who were normal weight and

overweight respectively (10). Highest risk for OSA in this study were seen in male, those aged ≥ 62 years, BMI ≥ 30 and T2D with history of snoring (10). This difference may be explained by the different tools of assessment and the small sample size in our study.

Our study showed that 53.2% screened high risk for OSA. Recent study of 330 adults with T2D who had overnight polysomnography showed that 49% of the men and 21% of the women participant have OSA (13). Recent study used Berlin questioner showed the prevalence of high OSA to be 65% with an estimated positive and negative predictive value of 68% and 22%, respectively (18).

Although our study showed that HbA1c was non-statistically different among those with high and low risk for OSA. A prospective study of 213 patients with OSA aged 27-80 years without history of DM were evaluated with fasting glucose (FBG) and for insulin resistance (HOMA-IR), they found that only patients with severe OSA significantly have higher FBG and higher HMOA-IR (15). Another study of 60 T2D patients that evaluated the impact of the OSA diagnosis and severity based on the HbA1c, showed linear trend of higher HbA1c with OSA diagnosis which correlated with OSA severity after adjusting of common variable like BMI, Age, sex and race (16). This discrepancy possibly related to the small sample size.

The presence of OSA in the T2D patients not only carries higher risk of uncontrolled diabetes but rather increase their existed risk of microvascular and macrovascular complications. Our study showed higher prevalence of microvascular complications in those who screened positive for OSA. Cohort of 118 T2D patients was evaluated to assess the relationship between OSA and retinopathy score and after adjusting for the confounding factors, it showed that retinopathy score were worse in T2D patients with OSA diagnosis (17).

Our study weakness includes the small sample size, single center and the lack of formal sleep study. Our strengths include comprehensive medical and laboratory data and using a validated questioner.

6. CONCLUSION

High risk diabetics for OSA tend to be older and have significantly higher BMI, systolic BP, resting heart rate, and tend to have significantly higher risk for neuropathy despite having non-significantly lower HbA1c.

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- **Author's contribution:** KA, MA, SA, AA: Contributed to conception and design. KA, MA, SA, AA: Acquisition of data. KA, MA: Analysis and interpretation of data. KA, MA, SA, AA: Drafting the article and revising it critically for important intellectualcontent. KA, MA, SA, AA: Final approval of the version to be published.

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