Stratification of Obstructive Sleep Apnea Risk in Obese non-Diabetics and Obese Diabetics

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Abstract

Introduction: The prevalence of OSA and its consequences are likely to increase in light of the current obesity epidemic. Studies have shown that the prevalence of OSA is significantly higher in the diabetes population. Recent studies have revealed that BMI and diabetes as significant independent predictors of OSA. Owing to little research in this field and lack of data from Central India, the present study aims at assessing the risk of development of obstructive sleep apnoea in obese and obese diabetic patients.

Objectives: To find out the prevalence of OSA risk in obese patients with Diabetes mellitus using Berlin Questionnaire, to find out the prevalence of OSA risk in obese non diabetic patients, correlation of OSA risk with Body Mass Index, fasting blood sugar, HbA1c and Blood Pressure.

Methodology: Twenty four obese diabetic patients (Group I) and thirty-five obese – non- diabetic patients (Group II) were selected from medicine OPD randomly. Results were matched with thirty-one healthy non-obese non-diabetic controls (Group III). Risk of OSA was assessed using pre designed, validated Berlin questionnaire. HbA1C and fasting blood sugars were done.

Results: As per Berlin Questionnaire Category 1 showed 19 (79.17%), 21 (60%) and 7 (22.58%) cases as positive in ‘DM and Obese’, ‘No DM but Obese’ and ‘Control’ groups respectively, P-value<0.0001 using Chi-square test. Category 2 had 7 (29.17%), 6 (17.14%) and 0 cases as positive in ‘DM and Obese’, ‘No DM but Obese’ and Control groups respectively with P-value of 0.008 (P<0.05) using Chi-square test and Category 3 had 18 (75%), 25 (71.4%) and 1(3.23%) positive cases in ‘DM and Obese’, ‘No DM but Obese’ and ‘Control’ groups respectively and the difference in the proportions was statistically significant with P-value<0.0001 using Chi-square test. Age above 40 years, female sex increased the risk of OSA. HbA1C was found out to be an independent risk factor for OSA risk. After adjusting for covariates for HbA1C, the OR obtained was 6.20 [95% CI: 1.37-28.07], with a P-value of 0.018 (P<0.05).

Conclusion: Our study shows that the risk of OSA is significantly increases with increasing BMI, fasting blood glucose levels, mean arterial pressure and HbA1c levels. High risk of OSA was 58.9% in our study.

Keywords: Diabetes mellitus; Obstructive sleep apnea; Pulmonary hypertension; Obesity; Hormone replacement therapy

Introduction

Obstructive sleep apnea (OSA) is a clinical condition characterized by repeated episodes of complete or partial obstruction of the upper airway during sleep, characterized by repeated episodes of complete or partial obstruction of the upper airway during sleep, associated with increased respiratory efforts, intermittent arterial oxygen desaturation, systemic and pulmonary arterial blood pressure alterations and sleep fragmentation. The cardinal symptoms of OSA are nocturnal respiratory pauses, interrupted by loud snoring and excessive daytime sleepiness. Obstructive sleep apnoea (OSA) adversely affects multiple organs and systems, with particular relevance to cardiovascular disease. Several conditions associated with OSA such as high BP, insulin resistance, systemic inflammation, visceral fat deposition and dyslipidemia are also present in other conditions closely associated to OSA and reduced sleep duration. It has been implicated in the etiology of hypertension and in the progression of several established medical conditions such as congestive heart failure, atrial fibrillation, diabetes and pulmonary hypertension [1]. In the adult population, the prevalence of OSA is estimated to be ~ 25% and as high as 45% in obese subjects. Obesity predisposes to and potentiates OSA [2]. The prevalence of OSA and its consequences are likely to increase in light of the current obesity epidemic. Studies have shown that the prevalence of OSA is significantly higher in the diabetes population [2,3]. Recent studies have revealed that BMI and diabetes as significant independent predictors of OSA [4]. The prevalence of OSA in obese or severely obese patients is nearly twice that of the normal weight adults. Studies show that patients with mild OSA who gain 10% of their baseline are at a sixfold-increased risk of progression of OSA [5], and...
an equivalent weight loss can result in a more than 20% improvement in OSA severity [6]. Owing to little research in this field and lack of data from Central India, the present study aims at assessing the risk of development of obstructive sleep apnoea in obese and obese diabetic patients.

Objectives

- To find out the prevalence of OSA risk in obese patients with Diabetes mellitus using Berlin Questionnaire
- To find out the prevalence of OSA risk in obese non diabetic patients
- Correlation of OSA risk with Body Mass Index, fasting blood sugar, HbA1c and Blood Pressure.

Methodology

The patients attending Diabetes OPD in Medicine department of NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Digdoh Hills, Hingna, Nagpur.

Study design: Cross-sectional study.

Study population: Twenty four obese diabetic patients (Group I) and thirty-five obese – non diabetic patients (Group II) were selected from medicine OPD randomly. Results were matched with thirty-one healthy non-obese non-diabetic controls (Group III).

Following inclusion-exclusion criteria were followed:

Inclusion criteria:

- For cases, with BMI more than 25 and diagnosed cases of Type-2 Diabetes mellitus with BMI>25.
- Those who were ready to give consent and comply with study procedures (age more than 18 years).

The patients with BMI less than 25, pregnancy, patients on antipsychotic drugs, psychiatric illness, thyroid dysfunction, liver and kidney disease, those on Hormone Replacement Therapy, any other endocrine disorder leading to obesity, and patients on weight reduction treatment were excluded from the study.

Sample size: 24 cases in obese – diabetic category (Group I), 35 cases in obese – non diabetic category (Group II) and 31 controls age and sex matched (Group III).

Tool for data collection: Pre designed, validated Berlin questionnaire.

Fasting blood sugar and HbA1c

Patients who met the inclusion and exclusion criteria were then administered the Berlin Questionnaire. It is a self-reported validated questionnaire consisting of three categories related to the risk of having sleep apnoea. Patients were then, classified into high risk and low risk based on their responses on the individual items and their overall scores in the symptom categories.

Statistical analysis

The statistical analysis was made by Qualitative categorical integrative analysis. Odds ratio was calculated.

Results

Table 1 provides the descriptive statistics for various demographic, clinical and metabolic parameters for subjects in three study groups i.e. Obese and DM, Obese but no DM and Control group. Gender distribution was also significantly different in all the three groups, as indicated by P-value<0.0001. The obese and no DM group had significantly higher number of females as compared to other groups.

Mean BMI across three groups also differed significantly as revealed by P-value<0.0001 using one-way ANOVA.

The mean systolic, diastolic and mean arterial pressure did not show significant difference across study groups as indicated by P-values 0.072, 0.186, 0.664 (P>0.05).
SBP in mmHg [Mean ± SD]  | 125.25 ± 18.24 | 119.11 ± 10.33 | 117.41 ± 9.98 | 0.072†
DBP in mmHg [Mean ± SD]  | 80.83 ± 10.59  | 81.37 ± 10.23  | 84.84 ± 5.69  | 0.186†
MAP in mmHg [Mean ± SD]  | 94.68 ± 10.65  | 93.01 ± 9.11   | 94.74 ± 6.15  | 0.664†
FBS mg/dl [Mean ± SD]    | 160.78 ± 116.34| 94.38 ± 18.57  | 88.35 ± 11.06 | <0.0001†
HbA1c [Mean ± SD]       | 8.08 ± 2.08    | 7.57 ± 9.67    | 4.94 ± 0.58   | 0.116†

†Obtained using Pearson’s Chi-square test; ‡Obtained using one-way ANOVA

Table 1: Descriptive statistics for different characteristics of subjects across three study groups.

Table 2: Comparison of Berlin scoring system across three study groups.
After adjusting for covariates, the OR obtained was 6.20 [95% CI: 1.37-28.07], with a P-value of 0.018 (P<0.05).

Increased fasting blood glucose levels also indicated increased odds in favour of 'high risk' of OSA (5.58 [95% CI: 2.00-15.56]) with a P-value of 0.001 (P<0.05). In the multivariate model, the variable was dropped due to its high correlation with HbA1c, resulting into multicollinearity effect.

| Parameter | Levels | No. of OSA/Total (%) | Odds ratio [95% CI]; P-value |
|-----------|--------|----------------------|----------------------------|
| **Age (years)** | <=40 | 16/53 (30.2) | 1 |
| | >40 | 21/37 (56.7) | 3.03 [1.26-7.28]; 0.017 |
| | Male | 10/36 (27.8) | 1.11 [0.26-4.69]; 0.89 |
| | Female | 27/54 (50.0) | 2.56 [1.05-6.58]; 0.035 |
| **Gender** | Control | 1/31 (3.2) | 1 |
| | No DM+Obese | 18/35 (42.9) | 26.95 [4.86-687.7];<0.0001 |
| | DM+Obese | 18/24 (75.0) | 71.34 [11.49 - 1933.2];<0.0001 |
| **Category** | Normal (70-100) | 27/75 (36.0) | 1 |
| | Above normal | 10/15 (66.7) | 3.55 [1.10-11.48]; 0.043 |
| **MAP (mmHg)** | Normal (<6) | 11/56 (19.6) | 1 |
| | Above normal (>6) | 26/34 (75.0) | 13.29 [4.74-37.27];<0.0001 |
| **HbA1c (%)** | Normal (<6) | 20/66 (30.3) | 1 |
| | Above normal (>100) | 17/24 (70.8) | 5.58 [2.00-15.56]; 0.001 |

1Using multivariate logistic regression; FBS was excluded from the model due to high correlation with HbA1c.

Table 3: Multivariate logistic regression to determine effect of various factors on risk of OSA.

The subjects were divided into high and low risk groups based on the categories as defined by the Berlin scoring system.

**Out of the total study samples (90) validated, we distributed them into two categories of the risk of OSA:**

1. High risk of OSA (53)=58.9%
2. Low risk of OSA (37)=41.1%

Patients who came under the high risk category were further advised to undergo complete OSA study.

**Discussion**

The present study examined for the prevalence of OSA risk in obese patients with diabetes and without diabetes and also established correlations of OSA risk with BMI, FBS (Fasting blood sugar), HbA1c and blood pressure using Berlin questionnaire. The Berlin Questionnaire is a validated tool with sensitivity of 69% and a specificity of 83% [7].

Our results suggest that fasting blood sugar, BMI and HbA1c have a significant risk of OSA in obese diabetic and obese non diabetic patients after adjusting for other variables with a p value of <0.0001, <0.0001 and 0.0116 respectively. Mean arterial pressure was associated with higher risk of OSA though not statistically significant. In addition, female sex and age above 40 years are other risk factors for OSA development.

Aronsohn found that Increasing OSA severity was associated with poorer glucose control, after controlling for age, sex, race, body mass index, number of diabetes medications, level of exercise, years of diabetes and total sleep time. This study is more extensive than ours as we have not taken into account the number of diabetes medications and the major difference being polysomnography which was done in all patients under the study. OSA severity positively correlated with increasing HbA1c levels. Our findings also suggest that HbA1C is an independent risk factor for OSA development [8].

Similar findings are reported regarding duration and quality of sleep and correlation with HbA1C levels [2] by another study. This study used the Pittsburgh Sleep Quality Index (PSQI) to assess the quality of sleep.

A different study showed the prevalence of OSA is significantly higher in diabetic population (p=-0.001). Multiple linear regression revealed BMI and diabetes as significant independent predictors of OSA [9]. These findings match with our study. However, there was a low correlation between OSA severity and HbA1c levels in the study sample whereas our study reports HbA1c as an independent risk factor for OSA.

Various abnormalities which include sleep fragmentation, reduced duration of slow wave sleep, increased sympathetic nervous activity,
intermittent hypoxia, poor sleep quality all can lead to dysregulation of glucose metabolism and diabetes over a period of time [10-15]. The association of HbA1c with OSA severity has many important implications in the clinical practice. It is not only the major target for prevention of complications in type 2 diabetes but it also represents a significant risk marker for cardiovascular disease in the general population. This fact enhances the increasing awareness that OSA itself is a risk factor for cardiovascular morbidity. Equally, HbA1c is also greatly appreciated as a risk marker for the development of diabetes in the general population. Hence, the severity of OSA may be associated with increased risk for development of diabetes. A study suggested that in non-diabetic males, the severity of OSA is associated with increased fasting glucose and HbA1c levels [1]. These findings clearly match with our study.

Many studies also depict correlation with blood pressure [9]. However, our present study depicts no significant correlation of OSA risk with mean arterial pressure though there is increasing risk with increase in can arterial pressure. This disparity could be due to lack of polysomnography data in our subjects.

OSA has been associated it a heightened systemic inflammatory state, as shown by increase in cytokines, serum amyloid A, and I some but not all studies, C-reactive protein. (15s) Subjects with OSA who received effective treatment with CPAP (continuous positive airway pressure) show improvement in the metabolic and inflammatory abnormalities. The close interactions between obesity, sleep deprivation and OSA share the common patho-physiologic feature of metabolic dysregulation. Weight loss may improve all of these conditions and might constitute an important potential intervention for these patients [16,17]. The limitations of our present report include the fact that we have not carried out the complete OSA study of the study subjects.

Conclusion

Our study shows that the risk of OSA is significantly increases with increasing BMI, fasting blood glucose levels, mean arterial pressure and HbA1c levels. High risk of OSA was 58.9% in our study.

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