

# The Impact of Obstructive Sleep Apnea Risk on Diabetic Retinopathy in Tabuk, Saudi Arabia

Hyder Osman Mirghani<sup>1)</sup>, Naif Mamdouh Alali<sup>2)</sup>

## ABSTRACT

**Background:** Diabetic retinopathy is a significant cause of blindness in Saudi Arabia and worldwide. One in five people in Saudi Arabia is suffering from diabetes mellitus. Obstructive sleep apnea and diabetes when co-exist aggravate each other with deleterious consequences. We aimed to assess the relationship between obstructive sleep apnea and diabetic retinopathy in Tabuk, Saudi Arabia

**Methods:** This is a sectional study conducted at the Diabetes Center in King Fahd Specialist Hospital, Tabuk City, Saudi Arabia during the period from August 2021 to February 2022. Two hundred and eight patients with type 2 diabetes were included. A structured questionnaire was used to collect socio-demographic and cardiovascular risk factors. Obstructive sleep apnea risk was assessed by the STOP-BANG questionnaire. The Statistical Package for Social Science was used for data analysis

**Results:** There were 208 patients with type 2 diabetes, their age was  $51.98 \pm 12.90$  years; the body mass index was  $32.28 \pm 9.38$ , the duration of diabetes was  $10.97 \pm 10.70$ , the Stop-Bang score ranged from 1-7 (mean  $\pm$  SD,  $4.37 \pm 1.61$ ) and the HbA<sub>1c</sub> was  $9.44 \pm 1.67$ . Obstructive sleep apnea was highly prevalent (84.6%) and diabetic retinopathy was evident in nearly half of the patients (48.1%). No significant statistical difference was evident between patients with and without retinopathy regarding obstructive sleep apnea risk ( $4.7 \pm 1.7$  versus  $3.9 \pm 1.4$ , 95% CI, -0.14-1.6, P-value, 0.093).

**Conclusion:** Obstructive sleep apnea and diabetic retinopathy were highly prevalent. No significant statistical association was evident between obstructive sleep apnea risk and diabetic retinopathy. Further larger multi-center studies are needed.

## KEY WORDS

obstructive sleep apnea, diabetic retinopathy, Tabuk, Saudi Arabia

## INTRODUCTION

Obstructive sleep apnea (OSA) is associated with various morbid disorders including cardiovascular diseases, diabetes mellitus, hypertension, and impotence.

OSA is also associated with increased healthcare utilization mainly from cardiovascular and all-cause mortality, in the Kingdom of Saudi Arabia 8.8% (12.8% in men and 5.1% in women) were suffering from the disease<sup>1)</sup>.

Worldwide, 93 million patients are suffering from diabetic retinopathy, of them; 28 million are vision-threatening diabetic retinopathy. Hypertension, diabetes duration, and poorly controlled diabetes are modifiable risk factors. Diabetic retinopathy is the leading cause of blindness with a great economic burden on the healthcare system<sup>2)</sup>.

Apnea/hypopnea index was not associated with diabetic retinopathy which was associated with a lower level of education<sup>3)</sup>, a study conducted in Singapore reported the association of apnea/hypopnea index with diabetic retinopathy and vision-threatening retinopathy<sup>3)</sup>, West *et al.*<sup>6)</sup> found an association between obstructive sleep apnea and diabetic retinopathy. Smith *et al.*<sup>7)</sup> in their retrospective study found that adherence to continuous positive airway pressure is beneficial in retinopathy reduction. Furthermore, apnea-hypopnea index during rapid eye move-

ment was shown to be associated with diabetic retinopathy in both home sleep apnea testing and all-night polysomnography<sup>8)</sup>. A high prevalence of microangiopathy was reported among patients with diabetes mellitus and OSA<sup>9)</sup>, Wong B and Fraser CL<sup>10)</sup> in their narrative review showed that OSA was associated with diabetes mellitus, diabetic retinopathy, and hypertension. Siwasaranond *et al.*<sup>11)</sup> thought that the link between OSA and diabetic retinopathy might be related to hypertension. A meta-analysis conducted in the year 2017<sup>12)</sup> pooled results from only six cohorts and showed the association between OSA and diabetic analysis. However, the limited databases included, the significant heterogeneity, and the methods and number of included studies (six case-control studies) limit its power to inform diabetes and ophthalmology communities regarding this important issue. OSA and diabetic retinopathy are common disabling disorders, when co-exist may aggravate each other with deleterious consequences. The earlier detection of diabetic retinopathy among patients with OSP will help the time management to reduce the lethal effects of both disorders. The association between OSA and diabetic retinopathy is controversial<sup>3)</sup>, no researchers have assessed this important issue in Saudi Arabia. Thus, we conducted this research to assess the relationship between OSA and diabetic retinopathy in Tabuk City, Saudi Arabia.

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1) Internal Medicine and Endocrine, Medical Department, Faculty of Medicine, University of Tabuk  
KSA

2) Ophthalmology, Department of Surgery, Faculty of Medicine, University of Tabuk  
KSA

Correspondence to: Naif Mamdouh Alali  
(e-mail: nmalali@ut.edu.sa)

**Table 1: Basic characters of the study group**

Character	Range	mean $\pm$ SD
Age	31-90	51.98 $\pm$ 12.90
Body mass index	16.2-56.80	32.28 $\pm$ 9.38
Neck circumference	34-54.5	40.93 $\pm$ 3.65
Obstructive sleep apnea score	1-7	4.37 $\pm$ 1.61
Duration of diabetes	1-50	10.97 $\pm$ 10.70
HbA1c	6.5-13	9.44 $\pm$ 1.67

**Table 3: The relationship of obstructive sleep apnea risk, retinopathy, and diabetes duration.**

Character	Retinopathy	No retinopathy	95% CI	P-value
Stop-Bang Score	4.7 $\pm$ 1.7	3.9 $\pm$ 1.4	-0.14-1.6	0.093
Duration of diabetes	13.48 $\pm$ 12.35	8.21 $\pm$ 8.39	-0.91-11.4	0.093

## SUBJECTS AND METHODS

This is a sectional study conducted at the Diabetes Center in King Fahd Specialist Hospital, Tabuk City, Saudi Arabia during the period from August 2021 to February 2022. Two hundred and eight patients with type 2 diabetes were included. The diabetes center is the only one in Tabuk City and serves around 15,000 patients with the diagnosis of diabetes mellitus. All adult patients with type 2 diabetes mellitus who came for their regular follow-up were approached, children and pregnant women, and other types of diabetes mellitus will be excluded

### Sample size:

The sample size for this study was obtained using the formula:  $Z^2 P-Q/d$ , where  $Z = 95\%$  confidence (1.96),  $P =$  the prevalence of diabetes in Saudi Arabia,  $d =$  and the margin of error = 0.05 = 208 patients.

### The research hypothesis:

Those at risk of obstructive sleep apnea are more prone to diabetic retinopathy and severe DR.

### Participants:

Adults with type 2 diabetes mellitus and coming for diabetes holistic care.

### Inclusion and exclusion criteria:

All adults with the diagnosis of type 2 diabetes mellitus were included, children and pregnant women, and other types of diabetes mellitus will be excluded.

### Measures:

A structured questionnaire was used to interview the participants depending on the Ministry of Education and Ministry of Health recommendations for infection control and social distancing during the time of the interview). The questionnaire consisted of two parts, sociodemographic factors and the STOP-BANG questionnaire for OSA risk assessment. The STOP-BANG questionnaire is an eight items (yes/no) and easy to use. The Arabic version questionnaire has been previously validated as an excellent screening tool for obstructive sleep apnea<sup>13</sup>. The questionnaire inquires about risk of obstructive sleep apnea, namely: age, sex, snoring, tiredness, observed apnea, hypertension, body mass index, and neck circumference<sup>14</sup>. The total score ranges from zero to eight. With a high sensitivity to detect both mild-moderate and severe OSA at score of  $\geq 3$ <sup>15</sup>.

Diabetic retinopathy was graded by an experienced Ophthalmologist as proliferative and background (mild, moderate, and severe)<sup>16</sup>.

**Table 2: Obstructive sleep apnea and comorbidities among patients with diabetes**

Character	No%
Obstructive sleep apnea	176 (84.6%)
Hypertension	96 (46.2%)
Snoring	44 (21.2%)
Fatigue	140 (67.3%)
Observed breathing	68 (32.7%)
Sex	96 (46.2%)
Neuropathy	56 (26.9%)
Retinopathy	100 (48.1%)
Exercise	60 (28.8%)
Coronary artery disease	44 (21.2%)
Dyslipidemia	120 (57.7%)

### Ethical consideration:

An approval letter was obtained from the Ethical Committee of the University of Tabuk (ref. UT-138-12-2021, dated, February 18, 2021) and all the patients signed a written informed consent.

### Statistical analysis:

The Statistical Package for Social Sciences (SPSS, IBM, and version 20, New York) was used for data analysis. The One-way Sample T-test was used to assess the relationship between OSA Score and diabetic retinopathy. A P-value of  $< 0.05$  will be considered significant.

## RESULTS

There were 208 patients with type 2 diabetes, their ages ranged from 31-90 years with a mean of 51.98  $\pm$  12.90 years; the body mass index was 32.28  $\pm$  9.38, the duration of diabetes was 10.97  $\pm$  10.70, and neck circumference 40.93  $\pm$  3.65. In this study, the Stop-Bang score ranged from 1-7 (mean  $\pm$  SD, 4.37  $\pm$  1.61) and the HbA1C was 9.44  $\pm$  1.67. Table 1.

Obstructive sleep apnea was highly prevalent (84.6%) and diabetic retinopathy was evident in nearly half of patients (48.1%), hypertension was found in 46.2%, loud snoring in 21.2%, and observed breathing in 32.7%. It is interesting to note that, more than two-thirds of patients suffered from fatigue (67.3%), and only 28.8% are on regular physical activity. Other co-morbidities and Stop-Bang score items were depicted in Table 2.

In the present study, the Stop-Bang score was higher among patients with diabetic retinopathy and prolonged diabetes duration (4.7  $\pm$  1.7 versus 3.9  $\pm$  1.4, 95% CI, -0.14-1.6, P-value, 0.093, and 13.48  $\pm$  12.35 years versus 8.21  $\pm$  8.39 years, 95% CI, -0.91-11.4 years, P-value, 0.093 respectively). Table 3.

## DISCUSSION

Previous meta-analysis of observational study conducted on the relationship between diabetic retinopathy and obstructive sleep apnea are contradicting with some showed a relationship<sup>17</sup>, and other failed to draw a conclusion<sup>3</sup>. The current study showed that patients with type 2 diabetes mellitus in Tabuk City, Saudi Arabia were at a high risk of obstructive sleep apnea and diabetic retinopathy. Obstructive sleep apnea score was higher among patients with DR. However, the results did not reach statistical significance. The present findings are in contradiction to a recent study published in India<sup>18</sup>, the authors showed a higher diabetic retinopathy among patients with moderate-severe OSA. A retrospective study conducted in the USA observed similar findings<sup>19</sup>. A longitudinal study conducted in the United Kingdom showed that OSA was associated with sight-threatening DR<sup>20</sup>. However, a recent case control study published in Belgium and a multi-center prospective study published in China showed no association<sup>21,22</sup>.

## Mechanisms of impact of obstructive sleep apnea and diabetic retinopathy:

The association between OSA and DR may be mediated by microangiopathy<sup>23</sup>. Increased blood vessels tortuosity and decreased vessels density in parafoveal and peripapillary areas was observed<sup>24</sup>. In addition, intermittent hypoxia may increase the risk of diabetes mellitus and lead to poor glycemic control<sup>25</sup>. Endothelial dysfunction, systemic inflammation, oxidative stress, and sympathetic drive are to blame<sup>26</sup>, increased levels serum vascular endothelial growth factors and reduced endothelial regulatory function was also suggested<sup>27</sup>.

## Conclusion:

Obstructive sleep apnea and diabetic retinopathy were highly prevalent. No significant statistical association was evident between OSA risk and DR. Further larger multi-center studies addressing the effects of obstructive sleep apnea on different grades of diabetic retinopathy are needed

## CONFLICTS OF INTEREST

None to declare.

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