

A Possible relation between Obstructive Sleep Apnea and Erectile Dysfunction: A Double-blinded Screening Observational Study

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Abstract: Objectives: To screen subjects seeking for medical advice for their obstructive sleep apnea (OSA) or erectile dysfunction (ED) who consider themselves healthy as regard to ED or OSAS, respectively for the prevalence of each disease among the other group. Patients & Methods: The study aimed to include all male patients attending Urology outpatient clinic with sexual problems without certain complaint or comment of their sleep behavior (Group A) and all patients attending Otorhinolaryngology outpatients clinic with snoring complaints without certain complaint or comment of their sexual function (Group B). Sleep problems assessment was conducted using a sleep questionnaire and subjects were categorized as heavy, moderate and none/mild snorers. Erectile function was assessed using the International Index of Erectile Function (IIEF-5) questionnaire for a total score of >25 is graded as normal erectile function (EF). Sexual function was assessed using the Brief Male Sexual Function Inventory (BMSFI). Results: The study included 494 clinic attendants Group B subjects had significantly higher mean body mass index. Among Group A 37 subjects were normal, 127 had mild, 54 had moderate and 29 had severe ED and according to OSAS questionnaire 116 subjects had low-probability of OSA, 69 had intermediate-probability and 62 had high-probability of OSA. Among Group B 155 subjects had low-probability of OSA, 53 had intermediate-probability of OSA and 39 had high-probability of OSA and according to IIEF questionnaire, 85 subjects were normal, 81 had mild ED, 53 had moderate ED and 28 had severe ED. There was negative significant correlation between OSAS grade and IIEF-5 score in attendants of both clinics. ROC curve analysis of OSAS grades as predictor for presence of ED showed that just presence of OSAS could be used as screening test for presence of ED among subjects not complaining of ED with area under curve of 0.329. Conclusion: OSAS could be considered as an underlying pathogenic factor for later development of ED in male OSAS patients. IIEF-5 is a valid screening tool for ED and must be implemented during evaluation of OSAS patients and sleep disorders evaluation must be considered for patients with ED.

[Mohamed F. Shindy; Ahmed A. Al-Shal and Mohamed Al-Azab **A Possible relation between Obstructive Sleep Apnea and Erectile Dysfunction: A Double-blinded Screening Observational Study.** Journal of American Science 2011; 7(10): 523-528]. (ISSN: 1545-1003). <http://www.americanscience.org>.

Keywords: Obstructive sleep apnea, erectile dysfunction, International index of erectile function-5

1. Introduction

Sexual problems are diffuse in both genders. Epidemiologic evidence seems to support a role for lifestyle factors in erectile dysfunction. Sexual dysfunction is a common health problem in middle-aged and elderly males. The prevalence of dysfunction increases steadily with age, and this condition may affect up to 10% of men in their 40's and up to 80% of men ages 70 and over. Sexual dysfunction can have a strong negative impact on the quality of life. Thus, it represents a significant health problem, and identification of potentially modifiable risk factors may be important for disease prevention and treatment^(1,2).

Obstructive sleep apnea (OSA) is also a very common disease, affecting 5% to 20% of the adult population⁽³⁾ and could potentially represent a risk factor for multiple metabolic dysfunction and disease states; **Chou et al.**⁽⁴⁾ reported a high prevalence of hyperlipidaemia in sleep-related breathing disorders with desaturation index a determining factor contributing to hyperlipidaemia and under-diagnosis of

hyperlipidaemia in OSAS is a critical problem. **Pedrosa et al.**⁽⁵⁾ found OSA is highly prevalent in patients with hypertrophic cardiomyopathy and it is associated with left atrial and aortic enlargement, also OSA is independently associated with atrial fibrillation, a risk factor for cardiovascular death in this population. **Kepez et al.**⁽⁶⁾ reported that the presence of OSA may contribute to coronary artery disease risk of patients in association with its severity and the association between OSA and subclinical atherosclerosis seems to be primarily dependent on age.

Multiple disease processes were documented to induce or be associated with erectile dysfunction and deterioration of sexual function satisfaction, **Huang et al.**⁽⁷⁾ reported that glycometabolic disorder and subclinical endothelial dysfunction may underlay organic ED in young ED patients without well-known related risk factors. **Qian et al.**⁽⁸⁾ found cervical spinal cord compression may be related with male erectile dysfunction besides motor and sensory dysfunctions. **Roumigué et al.**⁽⁹⁾ reported that men with idiopathic

Parkinson's disease had a severe sexual dysfunction. Some of these diseases may induced, complicated by or were concomitant with ED, so the present study aimed to screen subjects seeking for medical advice for their OSAS or ED who consider themselves healthy as regard to ED or OSAS, respectively for the prevalence of each disease among the other group.

2. Patients and Methods

The present study was conducted at Departments of Otorhinolaryngology and Urology, Benha University Hospital since Jan 2009 till Jan 2011 to include all male patients attending the outpatient clinic of Urology with sexual problems and accept to undergo the survey protocol (Group A) without certain complaint or comment of their sleep behavior. Also, all patients attending the outpatients clinic of Otorhinolaryngology with snoring complaints and accept to undergo the survey protocol (Group B) without certain complaint or comment on their sexual function.

All patients underwent determination of demographic data including age, sex, weight, height and BMI was computed as the ratio of body weight in kilograms divided by the square of height in meters ($=\text{kg}/\text{m}^2$) and ideal BMI was defined as $\text{BMI} \leq 25$ ⁽¹⁰⁾.

Sleep problems assessment was conducted using a sleep questionnaire consisted of 4 questions about snoring concerning presence, severity, frequency and whether snoring bothered others; 2 questions on breathing pauses concerning; presence and frequency and 2 questions on fatigue and sleepiness manifested

as lack of energy and falling asleep after dinner. Subjects were divided into three groups of snoring severity: heavy snoring (high-probability of OSA), moderate snoring (indeterminate-probability of OSA) and none/mild snoring (low-probability of OSA). Questionnaire categories are shown in table 1⁽¹¹⁾.

Erectile function was assessed using the International Index of Erectile Function (IIEF-5) which is a questionnaire that is frequently used to assess changes in erectile quality after therapeutic intervention. Quality of male sexual function is assessed in 5 domains, with 6 items that assess erectile function answered in a range of 0-5 for a total score of 30 with score >25 is graded as normal EF, scores ranged from 17-25 are rated as mild ED, scores ranged from 11-16 are rated as moderate ED, and scores ranged from 1-10 are rated as severe ED⁽¹²⁾.

Sexual function was assessed using the Brief Male Sexual Function Inventory (BMSFI). This validated questionnaire consists of 11 questions related to five sexual function domains: sexual drive, erectile function, ejaculatory function, sexual problem assessment and overall sexual satisfaction. All questions were scored from 0 to 4 with domain scores equaling the sum of the individual questions comprising the domain. The domain scores range from 0–12 for erectile function and sexual problem assessment, 0–8 for sexual drive and ejaculatory function and 0–4 for sexual satisfaction; categorical analysis was shown in table 2^(13,14).

Table (1): Sleep questionnaire categories⁽¹¹⁾

Category	Characters
Heavy snoring	Breathing pauses >2 times/week + Snoring bothersome to others, snoring louder than talking, lack of energy or falling asleep after dinner
Mild or none snoring	Breathing pauses 1-2 times/week + Snoring did not bother others, snoring quieter than talking, no lack of energy or falling asleep after dinner
Moderate snoring	Is intermediate between heavy and mild snorers

Table (2): Brief Male Sexual Function Inventory⁽¹³⁾

Sexual function domains	Number of questions	Scoring		Outcome score
		Per question	Total	
Sexual drive	2	0-4	0-8	≤ 2 = low libido
Erectile function	3	0-4	0-12	≤ 3 = erectile dysfunction
Ejaculatory function	2	0-4	0-8	≤ 3 = ejaculatory dysfunction
Sexual problem assessment	3	0-4	0-12	≤ 3 = sexual problems
Overall sexual satisfaction	1	0-4	0-4	≤ 1 = low sexual satisfaction

3. Results

The study included 494 clinic attendants with mean age of 34.5 ± 7.5 ; range: 23-54 years. There was non-significant difference between both clinic attendants as regards age, however, Group B subjects

had significantly higher body mass index (BMI) strata ($X^2=8.32$, $p<0.01$) with significantly higher mean BMI ($Z=5.457$, $p<0.001$), (Table 3).

Categorization of Urology clinic attendants according to IIEF questionnaire defined 37 (15%) normal personnel, 127 (51.4%) personnel had mild ED,

54 (21.9%) personnel had moderate ED and 29 (11.7%) had severe ED. Verification of these personnel according to OSAS questionnaire defined 116 (47%) personnel had low-probability of OSA, 69 personnel (27.9%) had intermediate-probability of OSA and 62 personnel (25.1%) had high-probability of OSA. Categorization of Otorhinolaryngology clinic attendants according to OSAS questionnaire defined 155 (62.8%) personnel had low-probability of OSA, 53 (21.5%) personnel had intermediate-probability of OSA and 39 (15.7%) personnel had high-probability of OSA. Verification of these personnel according to IIEF questionnaire defined 85 (34.4%) normal personnel, 81 (32.8%) personnel had mild ED, 53 (21.5%) personnel had moderate ED and 28 (11.3%) had severe ED (Table 4).

One hundred and thirty-nine personnel (28.1%) were satisfied by overall sexual function, 88 personnel (17.8%) reported that overall sexual function was satisfactory despite the partial satisfaction by intercourse, 73 personnel (14.8%) complained of weak-to-absent desire and if intercourse was committed is

partially satisfactory but they considered the overall sexual function is satisfactory, 85 personnel (17.2%) complained of weak-to-absent desire and if intercourse was committed is partially satisfactory without approaching orgasm and considered the overall sexual function is unsatisfactory and 109 personnel (22.1%) found the overall sexual functions are unsatisfactory. Number of personnel commenting to have satisfactory overall sexual function was significantly higher ($X^2=8.133$, $p<0.01$) in Group B compared to Group A (Table 5).

There was negative significant correlation between OSAS grade and IIEF-5 score in attendants of both clinics, however the correlation was more intimate in Urology clinic attendants, ($r=-0.465$, $p<0.001$) compared to Otorhinological clinic attendants, ($r=-0.374$, $p<0.001$), (Figs. 1 & 2). ROC curve analysis of OSAS grades as predictor for presence of ED showed that just presence of OSAS could be used as screening test for presence of ED among subjects not complaining of ED with area under curve of 0.329, (Fig. 3).

Table (3): Patients' age and body mass index data

			Group A		Group B	
			Frequency	Mean±SD	Frequency	Mean±SD
Age (years)	Strata	20-30	88 (35.6%)	26.7±1.9	83 (33.5%)	27.4±1.6
		>30-40	110 (44.6%)	34.4±1.4	118 (47.8%)	35.1±2.2
		>40-50	41 (16.6%)	45.8±2	34 (13.8%)	46±2.6
		>50	8 (3.2%)	51.3±0.5	12 (4.9%)	51.7±0.9
	Total	247 (100%)	34.1±7.4 (23-52)	247 (100%)	35±7.5 (25-54)	
BMI (kg/m ²)	Strata	<25	22 (8.9%)	24±0.7	0	0
		25-30	67 (27.1%)	28.8±1	36 (14.6%)	29±1.2
		>30-35	63 (25.5%)	32.3±1.4	94 (38.1%)	33±1.6
		>35-40	95 (38.5%)	37.4±1.1	112 (45.3%)	37±1.4
	>40	0	0	5 (2%)	41.2±1	
Total	247 (100%)	32.6±4.7	247 (100%)	34.4±3.4*		

Data are presented as numbers & mean±SD; percentages are in parenthesis

*: significant difference versus Group A

Table (4): Patients' distribution according to IIEF and OSA questionnaires scoring

		IIEF				Total
		OSA	Normal (score>25)	Mild ED (score=17-25)	Moderate ED (score=11-16)	Severe ED (score=1-10)
Urology clinic attendants (Group A)	Low-probability	26 (10.5%)	71 (28.7%)	15 (6.1%)	4 (1.6%)	116 (47%)
	Intermediate-probability	7 (2.8%)	38 (15.4%)	18 (7.3%)	6 (2.4%)	69 (27.9%)
	Heavy-probability	4 (1.7%)	18 (7.3%)	21 (8.5%)	19 (7.7%)	62 (25.1%)
	Total	37 (15%)	127 (51.4%)	54 (21.9%)	29 (11.7%)	247
Otorhinologic clinic attendants (Group B)	Low-probability	72 (29.2%)	53 (21.5%)	21 (8.5%)	9 (3.6%)	155 (62.8%)
	Intermediate-probability	11 (4.5%)	23 (9.3%)	13 (5.3%)	6 (2.4%)	53 (21.5%)
	Heavy-probability	2 (0.8%)	5 (2%)	19 (7.7%)	13 (5.3%)	39 (15.7%)
	Total	85 (34.4%)	81 (32.8%)	53 (21.5%)	28 (11.3%)	247 (100%)

Data are presented as numbers; percentages are in parenthesis

Table (5): Patients' distribution according to Sexual Function Assessment questionnaires scoring

Data	Group A		Group B	
	Frequency	Total score	Frequency	Total score
Normal sexual desire, satisfactory intercourse, normal orgasm, satisfactory overall sexual function	58 (23.5%)	26.8±2.9 (20-34)	81 (32.8%)	28.5±3.3* (20-36)
Normal sexual desire, partially satisfactory intercourse, normal orgasm, satisfactory overall sexual function	47 (19%)	24.3±3.1 (16-30)	41 (16.6%)	25.4±2.3* (18-31)
Weak sexual desire, partially satisfactory intercourse, normal	34 (13.8%)	21.5±3.4	39 (15.8%)	23.7±2.7*

orgasm, satisfactory overall sexual function		(15-26)		(18-29)
Weak sexual desire, partially satisfactory intercourse, no orgasm, unsatisfactory overall sexual function	48 (19.4%)	17±2.3 (13-23)	37 (15%)	19.6±2.9 (14-27)
Weak sexual desire, no orgasm, unsatisfactory overall sexual function	60 (24.3%)		49 (19.8%)	

Data are presented as numbers; percentages are in parenthesis

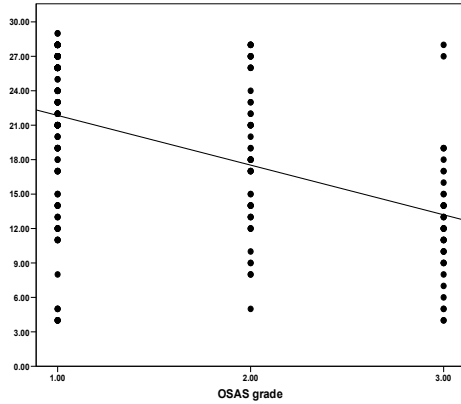


Fig. (1): Correlation between OSAS grade and IIEF-5 score in Otorhinological clinic attendants

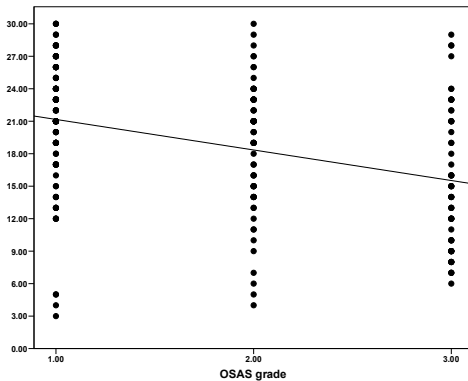


Fig. (2): Correlation between OSAS grade and IIEF-5 score in Urology clinic attendants

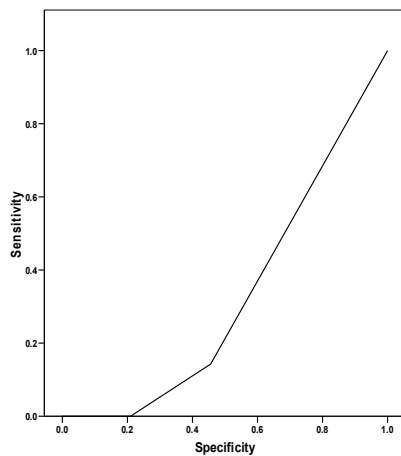


Fig. (3): ROC analysis of predictability of presence of OSAS for the presence of ED in studied population

Discussion

The current study was based on observational limited survey basis including attendants of both Urology and Otorhinolaryngology clinics provided that the attendants of each clinic had no definite complaint belonging to the other specialty. Both clinicians were blinded about the results of both questionnaires till fulfillment of targeted number of study participants.

The study relied on the International Index of Erectile Function (IIEF) for evaluation of erectile function and sexual satisfaction; such questionnaire is validated by multiple studies evaluating erectile function of various patients' population; **Coyne et al.** ⁽¹⁵⁾ analyzed the internal consistency of each of the five domains of IIEF and performed a factor analysis to confirm the domain structure of the questionnaire among patients with human immunodeficiency viral infection and found the internal consistency was high overall and concluded that this tool is suitable for evaluation of erectile function and can be used in screening, research, and monitoring treatment response. **Weiss & Brody** ⁽¹⁶⁾ examined associations of IIEF-5 scores with satisfaction aspects in both sexes and reported that for both sexes, greater IIEF-5 scores and penile-vaginal intercourse frequency plus vaginal orgasm consistency for women are associated with greater sexual and nonsexual satisfaction, and IIEF-5 scoring is a validated tool for both sexes.

The analysis of questionnaires outcome revealed high frequency of both morbidities among attendants of both clinics, a finding indicating an association between OSAS and ED and about 31% of Otorhinolaryngology clinic attendants without previous attending Urology clinic or requesting medical advice for sexual problems reported ED with overall sexual dissatisfaction on IIEF questionnaire despite this was not their driving motive to request medical advice, a finding indicating high frequency of ED among OSAS patients who were unaware of association between both morbidities and indicated the validity of IIEF questionnaire as a screening modality for ED irrespective of the clinical status of patients. These data go in hand with **Reis & Abdo** ⁽¹⁷⁾ who conducted a cross-sectional study including 288 male blood donors, aged between 40 and 60 years old aiming to define the prevalence of ED as defined by IIEF and reported a prevalence of ED of 31.9%, while self-reported ED prevalence was 3.1%. **Cruz et al.** ⁽¹⁸⁾ reported nocturia in 38%, nocturnal sweating in 34%, gasping in 30%, erectile dysfunction 25%, fatigue 23%, heartburn 15%,

and morning headaches 10% of subjects had moderate to severe OSAS and after 6 months of automatic positive air pressure (APAP) therapy, a statistically significant reduction on the prevalence of all symptoms was observed, except for erectile dysfunction and morning headaches. **Taskin et al.**⁽¹⁹⁾ found that after 1 month of regular CPAP usage, all OSAS subjects responded positively with mean value of IIEF-5 score was significantly improved and their erection status was improved positively, and concluded that a correlation between severe OSAS and ED was found and CPAP is effective in improvement of sexual performance of these patients.

There was a positive significant correlation between both morbidities; such association indicates a pathogenic relationship between both. However, considering OSAS as a chronic disease state that may date from childhood, thus it must play a role in development of ED with subsequent overall sexual function dissatisfaction. Moreover, ROC curve analysis found presence of OSAS could be considered as a sensitive predictor for ED, irrespective of severity of both entities. In hand with data, **Canguven et al.**⁽²⁰⁾ investigated the relationship between serum testosterone levels and erectile function was assessed by IIEF-5, and the severity of the disease in patients with OSA and found serum testosterone levels were negatively correlated with BMI and the severity of OSA and concluded that measuring testosterone level may be an additional helpful indicator in diagnosis of severity and in follow-up of OSA. **Hammoud et al.**⁽²¹⁾ found all parameters of sleep apnea including hypopnea index, percent time below a SpO₂ of 90%, and percent time below a SpO₂ of 80% were negatively correlated with testosterone levels and BMI and presence of coronary artery disease decreased the sexual quality of life, and concluded that sleep apnea was associated with reduced sexual quality of life and negatively affects testosterone levels independent of BMI. **Szymanski et al.**⁽²²⁾ investigated the prevalence of ED in ST-segment elevation myocardial infarction patients at high risk of OSA, and to evaluate the leading factors that increase the risk of ED and found ED was highly prevalent in these patients population at high risk of OSA and OSA was strong, independent risk factor for developing ED.

Multiple explanations were provided for the association between OSAS and ED; however, no definite pathogenic basis was settled. **Mohsenin & Urbano**⁽²³⁾ estimated serum levels of antiangiogenic proteins especially soluble fms-like tyrosine kinase-1 and soluble endoglin which are released under hypoxic stress conditions and cause endothelial dysfunction and reported significantly higher serum levels of both parameters in patients with OSA and hypertension and suggest that they may be involved in the pathogenesis

endothelial dysfunction and hypertension. **Rahangdale et al.**⁽²⁴⁾ reported that in obese patients with OSA, platelet activation is associated with greater levels of oxygen desaturation, compared with matched control subjects and the extent of hypoxemia may determine OSA-related thrombotic risk. **Ozeke et al.**⁽²⁵⁾ found that nocturnal mean and maximal heart rate to be associated with severity of OSA and the presence of hypertension and speculated that increased nocturnal mean and maximal heart rate caused by sympathetic nervous system activation in OSA might be one of the mechanisms in explaining the hypertension and OSA association.

In conclusion, OSAS could be considered as an underlying pathogenic factor for later development of erectile dysfunction in male OSAS patients. IIEF-5 is a valid screening tool for ED and must be implemented during evaluation of OSAS patients. On the other hand, sleep disorders evaluation must be considered during evaluation of patients with ED.

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10/24/2011