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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Comorbidities associated with obstructive sleep apnea: a retrospective Egyptian study on 244 patients

Rania Ahmad Sweed[1] · Salma Hassan[1] · Nashwa Hassan Abd ElWahab[1] · Soha Rashed Aref[2] · Mahmoud Ibrahim Mahmoud[1]

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Abstract

Purpose The aim of the present study was to assess prevalence of associated comorbidities in a group of patients diagnosed with obstructive sleep apnea syndrome (OSAS).

Methods This retrospective study enrolled 244 consecutive patients diagnosed by polysomnogram with OSAS between October 2010 and January 2015 after being referred to our Sleep-Related Breathing Disorders Unit, Chest Diseases Department, in the Alexandria Main University Hospital.

Results Of 244 patients, 47% were men, mean age was 56.9 years, and mean apnea–hypopnea index was 43.6 events per hour. Patients were categorized into two groups: group 1 (38%), mild and moderate OSAS, and group 2 (62%), severe, very severe, and extreme OSAS. Comorbidities were present in 91% of patients. The most common comorbidities were obesity, hypertension (HTN), and diabetes mellitus (DM). Prevalence of obesity, HTN, DM, congestive heart failure, deep vein thrombosis, pulmonary embolism (PE), and hypothyroidism was significantly higher in severity group 2. PE, bronchial asthma, and chronic obstructive pulmonary disease were significantly higher among men, whereas hypothyroidism was significantly higher among women. During this period of over 4 years, mortality rate was 8%. The majority of deaths occurred at night. Most of the studied patients (60%) either received no treatment or were not adherent to positive airway pressure (PAP) therapy. None of the patients received surgicaltreatment. The majority (50%) gained access to PAP therapy through donations. Associated hypoventilation was the only significant predictor of PAP adherence. Quality of life was significantly better among PAP adherent patients.

Conclusions Patients suffering from OSAS have very high prevalence of comorbidities indicating a great burden on the healthcare system. Despite this fact, over 50% of the patients studied did not receive any treatment. Charities were the main portal fortreatment.

Keywords Sleep apnea · Quality of life · Morbidity · Mortality · Comorbidity · PAP

Introduction

In recent years, the increasing prevalence of obesity has paralleled an increase in the prevalence of sleep apnea. In Egypt, the total prevalence rates of obstructive sleep apnea (OSA) and OSA syndrome (OSAS) are 14% and 4%, respectively [1]. Patients with untreated OSA are at increased risk of developing cardiovascular disease, resistant hypertension (HTN), type 2 diabetes mellitus (DM), and stroke. Among the US Medicare population with newly diagnosed heart failure (HF), those who were treated for OSA had better survival compared with those who were not treated. Only 2% of subjects with new-onset HF were tested for OSA over a 2-year period, yet the prevalence of OSA in HF has been reported to be approximately 50% [2]. In spite of this high prevalence of OSA, its impact on public health remains under-recognized. Proper diagnosis and treatment may decrease associated comorbidities and expenditures for care.

✉ Rania Ahmad Sweed
raniaswd@yahoo.com

[1] Department of Chest Diseases, Faculty of Medicine, University of Alexandria, 26 Mostafa kamel officer buildings, Alexandria, Egypt

[2] Department of Public, Preventive and Social Medicine, Faculty of Medicine, University of Alexandria, Alexandria, Egypt

Patients and methods

This study enrolled consecutive patients diagnosed with OSAS between October 2010 and January 2015 at our Sleep Related Breathing Disorders (SRBD) Unit, Chest Diseases Department, in Alexandria Main University Hospital. We enrolled patients with apnea–hypopnea index (AHI) ≥ 5, in the presence of symptoms suggestive of OSAS. Patients of both genders, 18 years of age and older, were included. Simple snorers with an AHI less than 5 and patients with airway tumors or craniofacial deformities were excluded. Patients or relatives of deceased patients were contacted by telephone and were invited to our hospital for assessment and clinical interview. Patients were subjected to history taking including symptoms relevant to SRBDs such as snoring, choking, witnessed apneas, non-refreshing sleep, recurrent arousals, morning headaches, and personality changes. Quality of life was assessed using the abbreviated World Health Organization quality of life (WHOQOL-BREF) questionnaire [3], The WHOQOL-BREF instrument is comprised of 26 items which measure the following broad domains: physical health, psychological health, social relationships, and environment. The WHOQOL-BREF is a shorter version of the original instrument. The short version may be more convenient for use in large research studies or clinical trials. Higher scores denote higher quality of life.

Patients were asked about comorbidities affecting cardiovascular, respiratory, endocrine, psychiatric, genitourinary, gastrointestinal systems, and malignancy. For diagnosis of comorbidities, we relied on documents presented by the patients regarding all diagnoses including previous investigations such as serial blood pressure measurements, fasting blood sugar, glycated hemoglobin, Free T3, T4, thyroid-stimulating hormone levels, electrocardiograms, echocardiograms, venous Doppler of the lower limbs, coronary angiograms, computerized tomography pulmonary angiography, and others tests, as well as detailed medical records of previous hospital admissions available in our hospital and discharge hospital records or reports from the intensive care unit (ICU). Date of disease onset and history of ICU admission were recorded. Details regarding the use of a positive airway pressure (PAP) device and adherence to PAP were based on self-report. Deaths were reported by direct contact with the patients' relatives including inquiry about time of death. Patients were subjected to physical examination and anthropometrics [weight, height, body mass index (BMI), and neck circumference (NC)]. Medical records and sleep studies were reviewed. Polysomnographic scoring was done in accordance with the American Academy of Sleep Medicine (AASM) published guidelines by trained pulmonologists.[5]

The ethics committee of our institution approved the study, and all participants gave their informed consent.

Statistical analysis

Descriptive statistics with means, median, and standard deviation were used to characterize the total population and subgroups. For analysis, we subdivided patients with OSAS into two groups: mild-moderate (AHI 5–30) and severe, very severe, or extreme (AHI > 30). [4] Data were analyzed using IBM SPSS software package version 20.0 (IBM Corp, Armonk, NY). Qualitative data were described using number and percent. The Kolmogorov–Smirnov test was used to verify the normality of distribution. Quantitative data were described using median and range or mean and standard deviation. Significance of the results was judged at the 5% level.

For between-group comparisons, chi-square test was used for categorical variables. Fisher's exact or Monte Carlo correction for chi-square was used when more than 20% of the cells had an expected count less than 5. Student's t test was used to compare groups of normally distributed quantitative variables. The Mann–Whitney test was used to compare groups of abnormally distributed quantitative variables. Multivariate logistic regression analysis was used to determine predictors of adherence to PAP therapy.

Results

Through patient record reviews, we found 600 patients referred to our SRBD Unit between October 2010 and January 2015. We were unable to contact a large portion of these patients due to changes in phone numbers. Ten patients were contacted but refused to join our study, and other patients were excluded because they did not match our inclusion and exclusion criteria (such as children and patients with craniofacial abnormalities)—see Fig. 1. We enrolled 244 patients in our study. Sociodemographic and anthropometric data are shown in Table 1. The AHI mean was 43.6 ± 26 events/h, with range 6 to 135 events/h and median 43 events/h. The age distribution for OSAS was as follows: 38% ≥ 60 years old, 24% (50 to 59), 24% (40to 49), 13% (30 to 39), and 2% (20 to 29) years old. The mean age of onset of SRBD was somewhat younger in men (43 ± 10 years) compared to women (46 ± 12 years, p = 0.014). For distribution of severity of OSAS see Fig. 2.

Associated comorbidities were revealed in 91% of patients. Specific rates of occurrence of comorbidities are shown in Fig. 3. Comparing groups by gender, pulmonary embolism (PE), bronchial asthma, and chronic obstructive pulmonary disease (COPD) were significantly higher in men, whereas hypothyroidism was significantly higher in women as shown in Fig. 4.

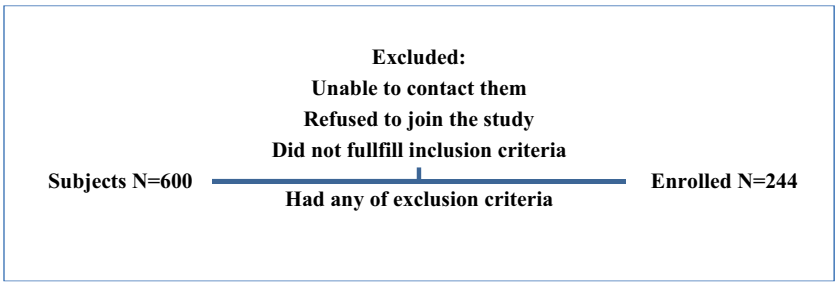

Fig. 1 Flow diagram of patients enrolled in the study

Comparing groups by severity, comorbidities occurred in 87% of group 1 patients versus 93% of group 2 patients ($p = 0.15$). Prevalence of obesity, DM, HTN, CHF, deep vein thrombosis (DVT), PE, and hypothyroidism were significantly higher in group 2 (Fig. 5). History of intensive care unit admission was reported by 23% of severity group 1 patients versus 48% of severity group 2 ($p < 0.001$). Frequency of ICU admission ranged from once to 8 times per year.

Overall mortality rate during the follow-up period of over 4 years was 8%, with mortality of 3% in severity group 1 versus 11% in group 2 ($p = 0.009$). Mortality rate was significantly higher in women (12%) versus men (3%, $p = 0.004$). The majority (79%) of deaths occurred at night. Sixty percent of patients either received no treatment or were never adherent to PAP therapy. Using multivariate logistic regression analysis, the only significant association with adherence to PAP therapy was hypoventilation syndrome (odds ratio 4.4, $p < 0.001$). Neither the comorbidities nor the polysomnographic parameters were predictive of adherence to PAP therapy. The remaining 40% of patients were adherent to PAP therapy (CPAP in 26% and bilevel PAP in 14%). None of our patients received surgical treatment for OSAS. Patients gained access to PAP devices by donation (50%), purchase (30%), health insurance (19%), or rental (1%). Quality of life was significantly better among patients adherent to PAP devices when compared to patients who received no treatment or those who were non-adherent in either severity groups ($p < 0.001$) as shown in Table 2.

Table 1 Distribution of the studied patients according to personal sociodemographic and anthropometric data ($n = 244$)

Personal and sociodemographic data	Number	Percent
Gender		
Male	115	47.0%
Female	129	53.0%
Age (years)		
Min.–max.	24.0–88.0	
Mean ± SD	56.92 ± 12.36	
Median	59	
Age of onset		
Min.–max.	14.0–75.0	
Mean ± SD	46.11 ± 11.98	
Median	48	
Marital status		
Single	10	5.3%
Married	232	93.4%
Divorced	2	1%
Family history of SRBD		
Negative	143	59%
Positive	101	41%
Smoking		
Non-smoker	181	74%
Smoker	36	15%
Ex-smoker	27	11%
Waist/hip ratio		
Min.–max.	0.08–1.96	
Mean ± SD	1.10 ± 0.24	
Median	1.07	
BMI (kg/m^2)		
Min.–max.	24.70–64.0	
Mean ± SD	42.6 ± 5.9	
Median	40	
Neck circumference (cm)		
Min.–max.	29.0–53.0	
Mean ± SD	43.55 ± 4.31	
Median	43	

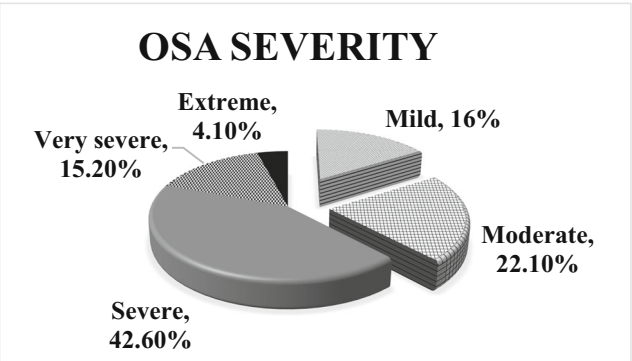

Fig. 2 Distribution of the patients according to apnea–hypopnea index ($n = 244$). For purpose of comparison, patients were categorized into two groups according to OSAS severity (group 1: mild and moderate) and (group 2: severe, very severe, and extreme)

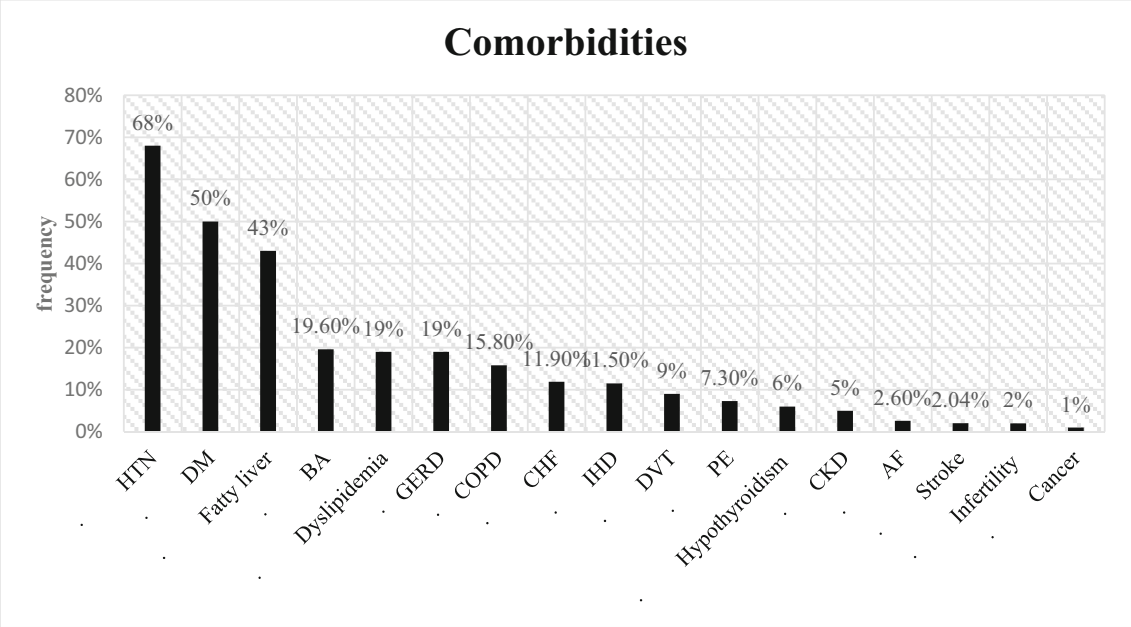

Fig. 3 Prevalence of different comorbidities ($n = 244$)

Discussion

Our study provides information about associations between OSAS and comorbidities. We found a substantial number of comorbidities with a higher frequency according to increased disease severity. We also found gender differences in the prevalence of some comorbidities. We attribute the high prevalence of comorbidities among our patients (over 90%) to the fact that the majority (62%) of patients were categorized as group 2 severity. This may be best explained by the nature of our referral population at our tertiary care hospital.

A previous Egyptian study reported 6-years' experience in an Egyptian sleep lab that enrolled 421 patients with 43% categorized as severe OSAS (AHI > 30). The authors attributed a late presentation of disease to lack of awareness as patients sought medical advice only when they experienced daytime sleepiness. This prior study did not address treatment, adherence to PAP devices, or the ways to obtain PAP devices. They reported the highest frequencies of comorbidities to be HTN (77%), DM (63%), and COPD (57%) but did not compare prevalence of comorbidities according to severity of disease or gender [5]. Surprisingly, in our study, the majority of

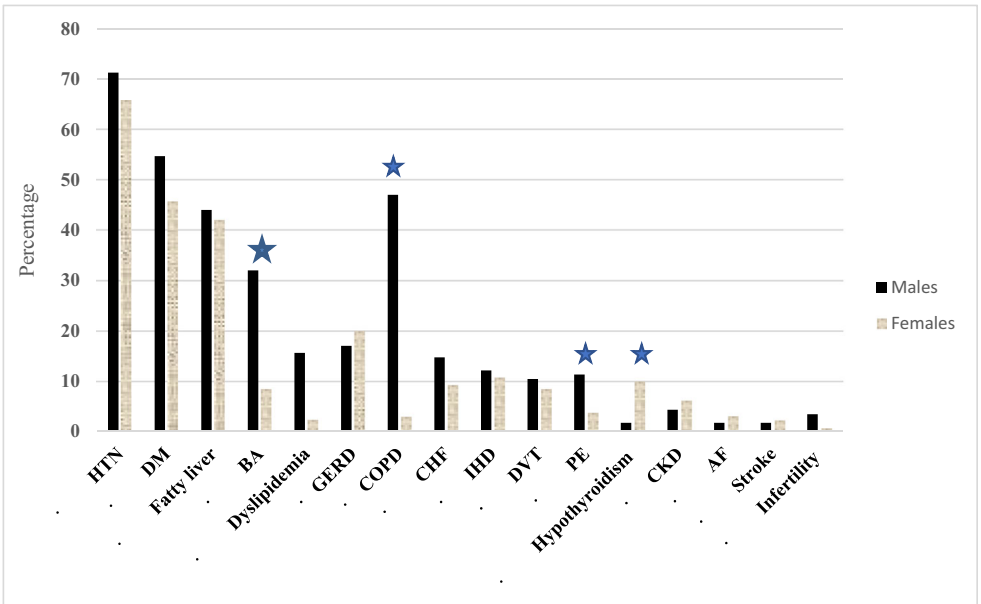

Fig. 4 Comparison of comorbidities between genders. Stars denote comorbidities with statistically significant differences

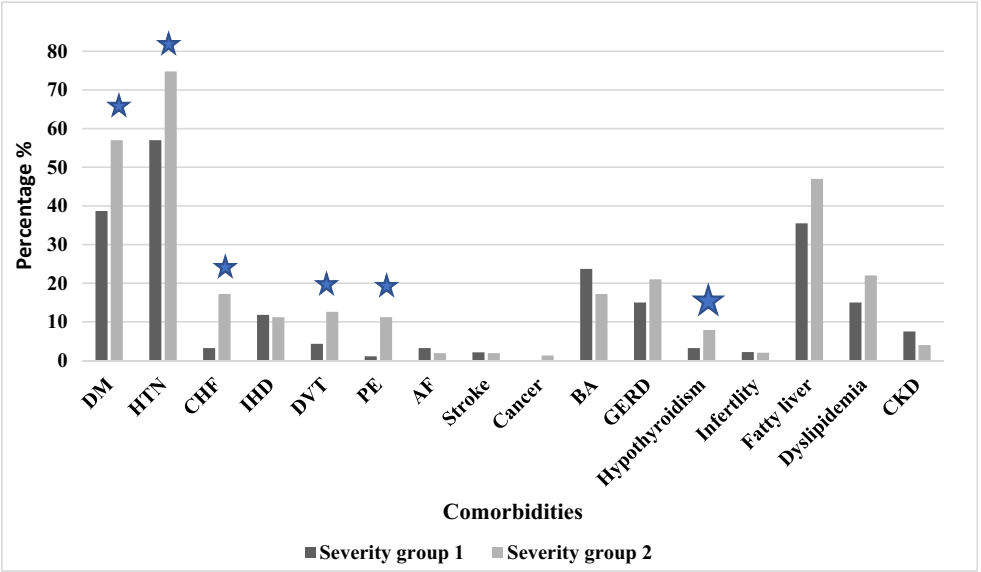

Fig. 5 Comparison of comorbidities between severity groups. Stars denote comorbidities with statistically significantly differences

patients who sought medical advice were women (53%). Another population-based study showed a 3-fold higher prevalence of OSAS in men [6]. We attribute our results to intolerance of male partners to female snoring considering it a social stigma resulting in higher presentation rates rather than prevalence rates in women.

Positive family history of SRBD was reported by 41% of studied patients. The high frequency of family history can be explained by a previous study that measured the size of upper airways using volumetric MRI showing family aggregation [7]. Asthma, COPD, and PE were more common among men, whereas only hypothyroidism was more common among women. Recently, in a study comparing the differences between 2052 men and 775 women with OSAS, it was shown that HTN, DM, thyroid disease, and asthma were more common in women [8].

In our study, obesity was the most common comorbidity followed by HTN and DM. Obesity was more common in severity group 2 (90%) compared to group 1 (77%, $p = 0.005$), but there was no significant difference between gender groups. These frequencies of obesity are consistent with another study reporting that over 70% of sleep apnea patients present with obesity [9]. A prospective study in Wisconsin residents showed that a 10% weight loss predicted a 26% decrease in sleep apnea severity [10]. All patients with obesity should be evaluated for OSAS and vice versa [11].

Prevalence of HTN was significantly higher in group 2 versus group 1 ($p = 0.004$), a finding that matches that of Lavie and coworkers who demonstrated linear increase in HTN with OSAS severity [12]. Among cardiac comorbidities, only HF was significantly higher in severity group 2 compared to group 1 patients. Similarly, a cross-sectional analysis of the Sleep Heart Health Study revealed that severe OSAS was associated with increased likelihood of HF (adjusted OR 2.20, 95% CI 1.11–4.37) [13]. The Wisconsin study showed that participants with untreated severe SRDB were 2.6 times

Table 2 Comparison of quality of life (WHOQOL-BREF score) between severity groups among surviving patients in relation to adherence ($n = 225$)

	SRBD severity degree				*t*	*p*
	Mild + moderate ($n = 90$)		Severe + very severe + extreme ($n = 135$)			
	Adherent ($n = 11$)	Not adherent ($n = 79$)	Adherent ($n = 77$)	Not adherent ($n = 58$)		
Quality of life score						
Min.–max.	87–114	64–100	65–98	55–86	601.739*	< 0.001*
Mean ± SD	96 ± 9.7	83 ± 12.5	89 ± 6.3	68 ± 9.1		
Median	92	77	90	65		

. $n = 225$, referring to patients who survived (244 − 19 deceased patients). *t*, *p*: *t* and *p* values for Student's *t* test for comparing between the two groups

more likely to have incident coronary heart disease or HF compared to those without SRDB [14]. Others have offered the controversial suggestion that the presence of OSAS might be protective in the setting of acute MI [15].

Atrial fibrillation was present in 2.6% of our patients almost matching the findings of the Sleep Heart Health Study which compared the prevalence of cardiac arrhythmias in subjects with or without SDB and reported AF prevalence rates of 4.8% and 0.9%, respectively ($P = 0.003$) [16]. More important is the increased frequency of nocturnal cardiovascular events and sudden cardiac deaths most likely secondary to arrhythmias which may explain the fact that 80% of our deceased patients died at night. This significant alteration in the day–night pattern of sudden death was evident in a previous study [17].

The third most frequent comorbidity is DM (57% in severity group 2, versus 39% in severity group 1, $p = 0.006$), a high rate in comparison to others estimating prevalence to be 15 to 30% [18]. We found no significant difference between gender groups unlike a previous study which revealed that the contribution of OSAS to DM development seems to be gender-dependent (higher in women) [19].

Hypothyroidism affected 6% of our patients, showing significant differences in both severity and gender groups: 7.9% in severity group 2 versus 3.2% in group 1 ($p = 0.03$), and 10.7% in women, versus 1.7% in men ($p = 0.007$). A previous study revealed a total prevalence of subclinical and clinical hypothyroidism in 13% of patients with OSAS, but there was no statistically significant correlation between thyroid functions and polysomnography findings.

It is worth noting that the majority of our patients either received no treatment or were not compliant to PAP devices. This fact raises question mark about the acceptance of PAP devices and the lack of proper counseling in our practice. In their study, Brian et al. showed that the rate of PAP adherence remains persistently low over 20 years despite efforts toward patient coaching. This low rate of adherence is problematic and calls into question the concept of PAP as gold standard of therapy for OSAS [20]. Frost and Sullivan estimates that out of the US adults diagnosed with OSA, approximately 85% receive the preferred treatment approach of PAP. However, only 60% will remain compliant with treatment protocols long term. Another difference in therapy between this study and ours is that in our population, patients received inadequate counseling and other lines of treatment were largely ignored, such as weight loss, lifestyle changes, positional therapy, oral appliance therapy, and surgery [21]. A review in the US reported that 16 of 22 studies (73%) showed worse PAP adherence in blacks compared to whites [22]. In our study, the association with hypoventilation syndrome was the only significant predictor of PAP adherence (OR 4.412, $p < 0.001$). Neither associated comorbidities nor polysomnographic parameters had significant effect on adherence. Similarly, May et al. did not identify any significant associations with polysomnographic metrics [23]. On the contrary, others have identified AHI as a predictor of PAP adherence [24]. Another study reported that the severity of OSA, subjective daytime sleepiness, and smoking status are independently related to adherence to CPAP therapy [25]. The American Academy of Sleep Medicine (AASM) released an analysis, "Hidden health crisis costing America billions." It was calculated that diagnosing and treating every patient in the USA with sleep apnea would produce an annual economic savings of $100.1 billion [22]. Walter et al. found a 33% reduction in non-sleep outpatient visits ($p < 0.01$) and a 17% decrease in laboratory studies ($p < 0.02$) [26].

The main strengths of this study are the large study population and the description of the local national experience. Regarding limitations, this is a cross-sectional design; hence, no cause-and-effect relationship could be determined. The effect of treatment on prevalence and severity of comorbidities was not addressed. Because of the lack of objective data from PAP devices (old versions of the devices), only subjective data regarding adherence was obtained. There was no adequate information obtained from patients regarding mental problems. Finally, it was not possible to precisely determine cause of death in deceased patients. Our study is a single-center study, and we urge all the Egyptian university sleep centers to pool their valuable data in a multicenter cohort to describe the pattern of SRBDs, prevalence, epidemiologic patterns, and comorbidities among Egyptians. It is a national problem to deal with awareness of OSAS and the logistical problems to supply appropriate therapy.

In conclusion, our study revealed high prevalence of associated comorbidities in patients with SRBD (≥ 90%). Nearly half of severity group 2 patients gave a history of ICU admission denoting high consumption of health services. Untreated sleep apnea increases the risk of costly health complications such as heart disease and diabetes. We cannot ignore the public health costs and burden of undiagnosed OSAS and its comorbidities. We aim to increase the portion of symptomatic patients diagnosed instead of dealing with the tip of the iceberg. This requires increasing awareness of the disease among the general population and among general practitioners. It is a striking fact that the majority of patients diagnosed with OSAS did not receive proper treatment and many patients denied receiving any advice regarding treatment options or potential risks of being not treated. The financial issues regarding treatment of OSAS are noteworthy in that half of treated patients gained access to PAP devices through donations.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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