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Sex differences in clinical and polysomnographic features of obstructive sleep apnea: The Turkish sleep apnea database (TURKAPNE) cohort

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ABSTRACT

Background: Previous reports from relatively small clinical cohorts have suggested that the clinical presentation of obstructive sleep apnea (OSA) differs between men and women.
Objective: We aimed to explore sex differences in clinical and polysomnographic features of OSA in a large nationwide registry.
Methods: Participants from the ongoing Turkish Sleep Apnea Database (TURKAPNE) Study from 34 centers were included in the current analysis. OSA was defined as an apnea-hypopnea index (AHI) ≥5 events/hour and was classified as mild, moderate, and severe according to AHI cut-offs 5, 15, and 30 events/hour, respectively.
Results: In all, 7130 patients (2259 women) were included. OSA was observed in 6323 (88.7 %), of whom 70.2 % were male and 29.8 % were female. In the OSA group, women were older (56.7 ± 11.9 *vs.* 49.5 ± 11.3 years; $p < 0.001$) and more obese (body mass index 34.3 ± 7.2 *vs.* 31.4 ± 5.6 kg/m^2; $p < 0.001$) and had lower AHI (29.8 ± 24.1 *vs.* 36.8 ± 26.2 events/h; $p < 0.001$) than men. Loud snoring and witnessed apnea were more common in men than in women whereas women were more frequently presented with insomnia, headache, and mood changes. Women had significantly less total sleep time, less sleep efficiency, and longer sleep latency compared with men ($p < 0.001$ for each). Additionally, comorbid diseases such as diabetes mellitus, hypertension, asthma, psychiatric disorders, hypothyroidism as well as drug use were more common in women than in men independent of age and obesity ($p < 0.05$ for each).
Conclusions: Our results suggest significant sex differences in clinical and polysomnographic features in this nationwide Turkish adult population. Women with OSA have more symptom burden and comorbidities despite having a less severe AHI.

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1. Introduction

Obstructive sleep apnea (OSA) is a prevalent condition with intermittent complete or partial obstruction of the upper airway followed by recurrent hypoxia and sleep fragmentation during sleep [1,2]. Globally, OSA has been estimated to affect almost one billion individuals aged 30–69 years, based on the apnea-hypopnea index (AHI) threshold of 5 events/h [3]. To date, there is yet no data regarding the occurrence of OSA in Türkiye based on polysomnography (PSG) studies. According to a survey-based study, Turkish Adult Population Epidemiology of Sleep (TAPES), including a nationwide representative sample of 5021 participants, the estimated OSA prevalence based on the Berlin Questionnaire has been reported as 14 % [4].

Individuals with OSA present typical symptoms such as loud snoring, witnessed apneas and excessive daytime sleepiness. Notwithstanding, nocturia, nocturnal sweating, headache in the morning, and difficulties in concentration as well as depressive mood are also reported [5–12]. OSA may lead to impaired daytime function, metabolic dysfunction, increased risk of cardiovascular disease, traffic accidents, and mortality, and undiagnosed and untreated OSA is a significant burden on the healthcare system [13–15].

OSA generally has been considered as a male disease. Prevalence of OSA with a male-to-female ratio is 4:1–6:1 in clinic-based studies while community-based epidemiological studies have reported 2–4/1 as a male/female prevalence ratio [2,16–18]. The sex difference decreases following menopause [19]. It has been proposed that upper airways are more collapsible in men [20]. It has also been suggested that apnea episodes are shorter, and hypopneas are more common than apneas, and rapid eye movement (REM) predominant OSA is more frequent in women than in men [21]. It has been argued that female patients with OSA are underdiagnosed and treatment is frequently delayed [5,6], which has been attributed to the differences in the clinical presentation of OSA [5–13,22–24]. Two previous reports from Türkiye have addressed the sex differences in OSA between Turkish men and women [11,12]. The sample size was relatively small, and home sleep apnea test (HSAT) was used as diagnostic tool in one of them [12], and the other one was a retrospective cohort study including 2827 patients with OSA [11]. Given that sociocultural status and the geographical distribution of participants could influence clinical presentation and symptom perception of OSA, a more detailed information in this context is urging.

In the current prospective study, we aimed to investigate sex differences in OSA severity, symptoms, comorbidities and polysomnographic features in a large nationwide registry.

2. Material-methods

2.1. The study population

The rationale and the design of the Turkish Sleep Apnea Database (TURKAPNE) study has previously been published [25]. In summary, the TURKAPNE study is an ongoing national, multicenter, observational, prospective cohort study, which was started in October 2017. Adults with suspected OSA who are referred to the sleep centers are invited to participate in the study. In all, 34 sleep centers have been participating (Fig. 1 – Türkiye map). Study with available demographics, anthropometric measurements (height, weight, body mass index [BMI], circumferences of the neck, waist, and hip), questionnaires, comorbidities and polisomnographic data from 34 centers were included in the current analysis. Patients with limited life expectancy due to advanced renal disease or uncontrolled malignancies, alcohol dependency and using mandibular advancement devices or positive airway pressure therapy were excluded.

2.2. Ethical considerations

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Ethics Committee of the Medical Faculty of the Marmara University, Istanbul (approval nr: 09.2016.311). All patients provided written informed consent. The study was registered with the Clinical Trials. gov (NCT02784977).

2.3. Data collection and data quality assurance

The TURKAPNE project uses a precisely designed web based data collection system constructed for transferring data to the central database www.turkapne.org at a server hosted by Hetzner Online GmbH localized in Jestetten, Germany [25]. Each center has a personal login to a clinical report format module containing predefined submodules for recording data. Each sleep center has complete access to data on its own patients. The registry of the participants is coded and the identity of the patients is kept at the reporting sleep center and secured with a written

Fig. 1. The map of Türkiye representing the cities with participating sleep centers.

participant identity log. Data quality is randomly checked by an independent data monitoring board with full access to the complete database.

2.4. Demographic and anthropometric data, comorbidities and concomitant medications

When logging into the system, information on age, gender, marital and educational status, driver's license, smoking and alcohol habits, height, weight, neck circumference, waist/hip circumference, heart rate and systemic blood pressure at the time of diagnosis, comorbidities, concomitant medications and information of menstrual/menopause status in women were recorded.

2.5. Excessive daytime sleepiness

Epworth Sleepiness Scale (ESS) consists of eight self-rated items and assesses the probability of dozing using a scale ranging from 0 (never) to 3 (high). The sum of each item score yielded a global score (range, 0–24). ESS assesses the risk of sleepiness in which patients with scores above 10 were considered as having significant daytime sleepines and high risk for OSA [26]. Sleepiness was assessed by the Turkish version of the ESS [27].

2.6. Polysomnographic findings

All patients underwent PSG for at least 7 h, and the use of coffee, alcohol, sedatives was banned on the same day. Indicators such as electroencephalogram, electromyography, blood oxygen saturation, electrooculogram, electrocardiogram, snoring, mouth airflow, nasal airflow, chest breathing and body position were included the monitoring. Polysomnography data contain total sleep time, sleep efficiency, sleep latency, REM latency, sleep stages, AHI, oxygen desaturation index (ODI), average and minimum oxygen saturation levels, time spent below 90 % oxygen saturation (T90 %), arousal index, periodic limb movement index, and heart rate. It was also detected sleep breathing disorders during supine/non-supine position and during the REM and non-REM sleep stages. Sleep staging and respiratory event scoring was in accordance with the latest guidelines [28,29]. Apneas were scored when there was a ≥90 % reduction in airflow amplitude for ≥10 s. Hypopneas were scored where there was a ≥30 % reduction in airflow amplitude for ≥10 s, accompanied by either an arousal or desaturation of ≥3 %. We defined OSA as an apnea–hypopnea index (AHI) ≥5event/hour, and moderate-to-severe OSA as an AHI ≥15event/hour, and a severe OSA as an AHI ≥30event/hour [30].

2.7. Statistics

Statistical analysis was performed with IBM SPSS 28.0 for Windows packaged software. Numerical variables were reported with mean ± standard deviation and categorical variables with frequency and percentage. The significance of differences among groups was assessed by Student-t test, and Chi-square test was applied for analysis of categorical variables. A value of $p < 0.05$ was considered significant. Multiple logistic regression analysis was used to determine the relationship between comorbidities and clinical symptoms with female sex, and odds ratio (OR) and 95 % confidence intervals (CI) were presented.

3. Results

Out of 7130 patients who fulfilled the inclusion criteria, 2259 (31.7 %) were women. As presented in Fig. 2, OSA was observed in 6323 (88.7 %) participants, of whom 70.2 % were male and 29.8 % were female. The rate of OSA was significantly higher in men compared with women (91.1 % vs. 83.4 %, respectively, $p<0.001$). Moreover, OSA was more severe in terms of AHI in a dose-response manner in men, whereas the rates of mild, moderate and severe OSA were similar in women (Fig. 2).

As shown in Table 1, women with OSA were older and more obese than men at the time of OSA diagnosis, and ESS scores were slightly higher in man compared with women (8.5 ± 5.8 vs. 7.7 ± 5.6, respectively, $p<0.001$). Proportion of married participants, education level, proportion of smokers and alcohol consumers were higher among men compared to women, Comorbid diseases such as diabetes mellitus, hypertension, asthma, arrhythmia, psychiatric disorders, hypothyroidism were more common in women than in men (Table 2). The use of drugs was much more common in women supporting the increased disease burden. In a logistic regression analysis, female sex was significantly associated with all aforementioned combordities indepent of age and obesity (Table 3). Arrhytmia was age-dependent.

The distribution of symptoms that were reported as "often" or "very often" is illustrated in Fig. 3, and odds ratios for symptoms associated with female *vs*. male sex are shown in Table 4. Thus, the symptom presentations differed significantly in many items, *i.e.,* loud snoring and witnessed apnea were more common in men than in women, whereas women were more frequently presented with insomnia, headache, and mood changes.($p<0.001$ for each).

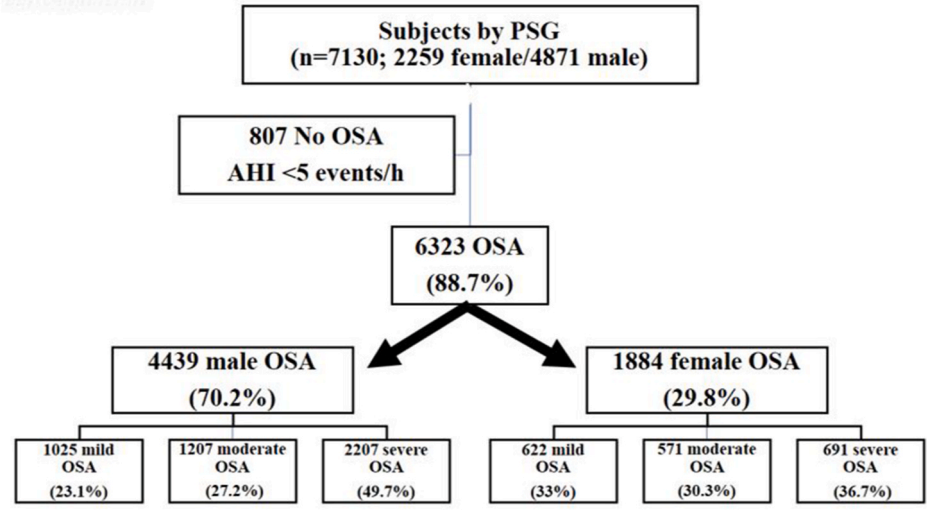

Fig. 2. Flow chart of the study cohort. *Abbreviations:* OSA, obstructive sleep apnea; PSG, polysomnography.

Table 1
Characteristics of the female and male participants with OSA (n = 6323).

	Female (n = 1884)	Male (n = 4439)	*p* Value
Age (years)	56.0 ± 11.3	49.5 ± 11.9	**<0.001**
	34.4 ± 7.2	31.4 ± 5.6	**<0.001**
BMI (kg/m^2)			
	7.7 ± 5.6	8.5 ± 5.8	**<0.001**
ESS score			
	1481 (78.6)	3878 (87.4)	**<0.001**
Civil status/married, n (%)			
Education Level			
No education, n (%)	336 (17.8)	324 (7.3)	**<0.001**
Primary School, n (%)	784 (41.6)	1110 (25)	
Secondary School, n (%)	151 (8)	542 (12.2)	
High School, n (%)	317 (16.8)	1165 (26.2)	
University, n (%)	296 (15.7)	1298 (29.2)	
Smoking			
Never smoker, n (%)	1134 (60.2)	1473 (33.2)	**<0.001**
Former smoker, n (%)	395 (21)	1369 (30.8)	
Current smoker, n (%)	355 (18.8)	1597 (36)	
Alcohol			
Never, n (%)	1795 (92.1)	3199 (72.1)	**<0.001**
Occasionally, n (%)	63 (3.3)	295 (6.6)	
Once a month, n (%)	50 (2.7)	418 (9.4)	
Once a week, n (%)	25 (1.3)	314 (7.1)	
Several times a week, n (%)	5 (0.3)	151 (3.4)	
Every day, n (%)	6 (0.3)	62 (1.4)	

Data are expressed as mean ± SD unless otherwise stated.
Abbreviations: BMI, body mass index; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea.

Table 2
Comorbidities and drugs of the female and male participants with OSA (n = 6323).

	Female (n = 1884)	Male (n = 4439)	*p* Value
Comorbidities			
Diabetes mellitus, n (%)	474 (25.2)	671 (15.1)	**<0.001**
Hypertension, n (%)	801 (42.5)	1297 (29.2)	**<0.001**
Asthma, n (%)	295 (15.7)	305 (6.9)	**<0.001**
COPD, n (%)	44 (2.3)	180 (4.1)	**0.001**
Coronary artery disease, n (%)	79 (4.2)	209 (4.7)	0.392
Congestive heart failure, n (%)	71 (3.8)	124 (2.8)	**0.046**
Arrhythmia, n (%)	117 (6.2)	175 (3.9)	**<0.001**
Stroke, n (%)	15 (0.8)	33 (0.7)	0.874
Psychiatric disorders, n (%)	119 (6.3)	143 (3.2)	**<0.001**
Hypothyroidism, n (%)	138 (7.3)	62 (1.4)	**<0.001**
Medications			
Antihyperlipidemic drugs, n (%)	96 (5.1)	240 (5.4)	0.668
Inhaled medications, n (%)	122 (6.5)	199 (4.5)	**0.001**
Montelukast, n (%)	23 (1.2)	34 (0.8)	0.083
Antihistamine, n (%)	37 (2.0)	57 (1.3)	0.053
Insulin, n (%)	41 (2.2)	67 (1.5)	0.071
Oral antidiabetics, n (%)	278 (14.8)	448 (10.1)	**<0.001**
Thyroid medications, n (%)	189 (10.0)	87 (2.0)	**<0.001**
Beta-blockers, n (%)	262 (13.9)	439 (9.9)	**<0.001**
Calcium channel blockers, n (%)	141 (7.5)	228 (5.1)	**<0.001**
ACE inhibitors, n (%)	137 (7.3)	269 (6.1)	0.073
Angiotensin receptor blockers, n (%)	85 (4.5)	152 (3.4)	**0.042**
Diuretics, n (%)	71 (3.8)	107 (2.4)	**0.004**
Alpha blocker drugs, n (%)	26 (1.4)	67 (1.5)	0.733
NSAI drugs, n (%)	15 (0.8)	19 (0.4)	0.089
Proton pump inhibitors, n (%)	95 (5.0)	162 (3.6)	**0.012**
Aspirin, n (%)	137 (7.3)	309 (7.0)	0.668
Clopidogrel, n (%)	18 (1.0)	64 (1.4)	0.144
Warfarin, n (%)	10 (0.5)	15 (0.3)	0.276
Psychiatric drugs, n (%)	219 (11.6)	196 (4.4)	**<0.001**
Antiepileptic drugs, n (%)	16 (0.8)	35 (0.8)	0.878

Data are expressed as mean ± SD unless otherwise stated.
Abbreviations: ACE, Angiotensin converting enzyme; COPD, chronic obstructive pulmonary disease; NSAI, Nonsteroidal anti-inflammatory; OSA, obstructive sleep apnea.

Table 3
Odds ratios for comorbidities associated with female sex in a multivariate logistic regression analysis adjusted for age and obesity.

Symptoms	Odds Ratio	95 % Confidence Interval	*p* Value
Diabetes mellitus	1.4	1.18–1.57	**<0.001**
Hypertension	1.2	1.05–1.36	**0.006**
Asthma	2.3	1.93–2.77	**<0.001**
Arrythmia	1.2	0.91–1.54	0.201
Psychiatric disorders	2.3	1.72–2.94	**<0.001**
Hypotyrodism	5.2	3.74–7.21	**<0.001**

As shown in Table 5, AHI as well as ODI was significantly elevated in men, whereas women had significantly less total sleep time, less sleep efficiency, and longer sleep latency than men ($p < 0.001$ for each).

When comparing the cohort stratified by the age of 50, as a cut-off for postmenopausal status in women, the occurrence of OSA was higher in the male patients younger than 50 years of age compared with premenopausal female patients (88.1 % vs. 69.1 %; $p < 0.001$). The occurrence was still higher among men above 50 years old than postmenopausal women but the difference was quite small though it was significant (95.2 % vs. 91.2 %; $p < 0.001$). Additionally, OSA severity in women before and after menopause was evaluated and it was found that postmenopausal women had significantly higher AHI (29.9 ± 24.4 *vs.* 16.9 ± 21.7, $p < 0.001$) and ODI (33.4 ± 43.3 vs. 18.8 ± 34.4, $p < 0.001$) than those before menopause.

4. Discussion

This article has reported several features concerning the clinical presentation and polysomnographic findings of OSA in Turkish male and female patients from the ongoing TURKAPNE Study.

To our best knowledge, this is the first, largest, prospective, nationwide cohort study regarding the sex differences in OSA severity, symptoms and comorbidities. We showed that loud snoring and witnessed apnea were more common, and the disorder was more severe in terms of AHI and ODI in men than in women, whereas women were older at the time of the OSA diagnosis and presented more comorbidities in terms of obesity, diabetes mellitus, hypertension, asthma, arrhythmia, psychiatric disorders and hypothyroidism. Thus, there were significant sex-differences and miss-match between the AHI severity and the symptom severity as well as comorbidities.

Previously, two single-center studies from Türkiye reported sex differences in OSA. In the study of Basoglu et al. [11], including 2827 OSA patients, women were also older and more obese, presenting atypical symptoms compared with the men. Comorbidities such as hypertension, diabetes mellitus, hypothyroidism and asthma were also more common in females. In another study, reported by Bostan et al. [12], OSA was prevalent among 589 adults based on home sleep apnea test recordings, and again, women were older and and more obese than men. Women presented more commonly with daytime fatigue, nocturia, headache in the morning, depressive mood and restless legs symptoms than did men. Thus, our current results confirm these previous findings and expand these results to be representative nationwide. One may argue that age and obesity may explain these sex differences. However, our results suggest that the majority of these comorbidites occur in women with OSA independent of age and obesity.

In literature, a few other studies addressed the sex differences in OSA in clinical cohorts. In a retrospective study in China, 580 patients with OSA were evaluated [7]. There were no significant difference in age at diagnosis but women complained more about insomnia, poor sleep quality and headache on awakening than men, while men more commonly reported snoring compared with women. Another retrospective study in Greece included 1010 patients with OSA and found no significant difference in BMI between men and women [22]. Thus, there might be ethnical, cultural and racial differences regarding sex differences in this research area.

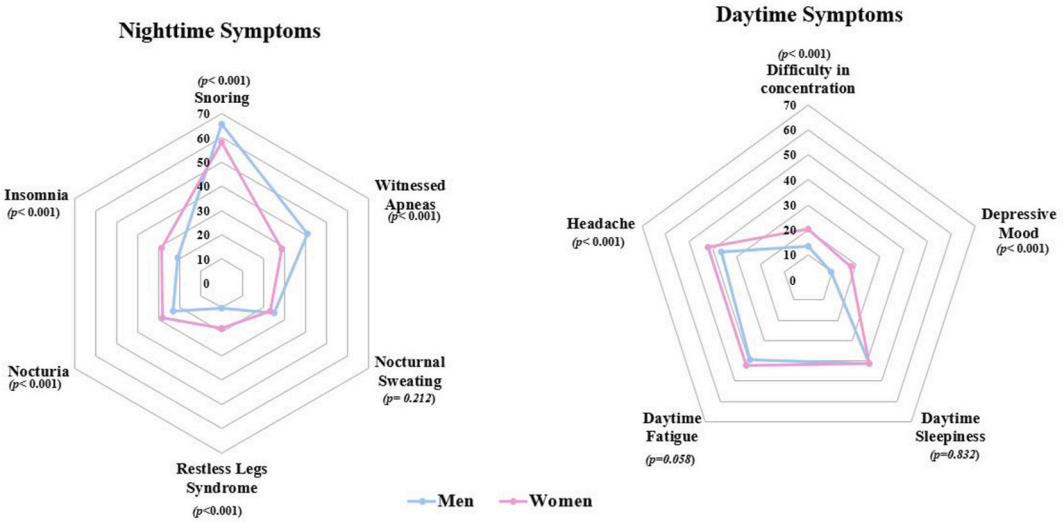

Fig. 3. Radar plot of the distribution of symptoms in female and male patients with OSA. *Abbreviation:* OSA, obstructive sleep apnea.

Table 4
Odds ratios for symptoms associated with female sex in a multivariate logistic regression analysis adjusted for age and body-mass-index.

Symptoms	Odds Ratio	95 % Confidence Interval	*p* Value
Snoring	0.6	0.54–0.71	**<0.001**
Witnessed apnea	0.5	0.43–0.59	**<0.001**
Daytime sleepiness	0.9	0.80–1.05	0.2
Daytime fatigue	1.0	0.90–1.19	0.6
Headache	1.2	1.06–1.40	**0.005**
Insomnia	1.4	1.19–1.62	**<0.001**
Nocturia	0.9	0.75–1.02	0.1
Difficulty in concentration	1.7	1.43–2.05	**<0.001**
Depressive mood	1.9	1.57–2.33	**<0.001**
Restless leg syndrome	1.7	1.43–2.10	**<0.001**

Table 5
Polysomnographic parameters of the female and male participants with OSA (n = 6323).

	Female (n = 1884)	Male (n = 4439)	*p* Value
AHI, events/h	29.8 ± 24.1	36.8 ± 26.2	**<0.001**
ODI, events/h	32.9 ± 43	38.8 ± 51.3	**<0.001**
TST, min	370.4 ± 77.7	378.4 ± 74.4	**<0.001**
Sleep efficiency, %	81.2 ± 15.8	83.7 ± 17.7	**<0.001**
Sleep latency, min	30.4 ± 33.6	22.4 ± 26.7	**<0.001**
REM, % of TST	13.9 ± 7.7	14.2 ± 9.5	**0.09**
N3, % of TST	25.4 ± 16.4	22.5 ± 15.2	**<0.001**
Mean SpO_2,%	92.4 ± 5.5	92.6 ± 5.2	0.1
Minimum SpO_2,%	78.4 ± 11.0	78.4 ± 11.4	0.95
T90, %	7.7 ± 5.6	8.5 ± 5.8	0.2
Mean pulse, min	70.2 ± 14.9	68.2 ± 13.5	**<0.001**

Data are expressed as mean ± SD unless otherwise stated.
Abbreviations: AHI, apnea hypopnea index; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; REM, rapid eye movement; SpO_2, saturation measured by oximeter; T90, percentage of sleep time with SpO_2 below 90 %; TST, total sleep time.

Previous studies have shown that menopause is a risk factor for OSA in women [18]. For this reason, we think that in many studies like ours, women diagnosed with OSA are older than men with OSA. Prevalence of OSA in women doubles after menopause independently of age and BMI [31]. Our results support these findings and additionally suggest that OSA is more severe after menopause in terms of AHI. Premenopausal women have been suggested to be protected from OSA with more stable respiratory effort in non-REM sleep in response to arousals and hypercapnia [32]. During the menopausal period, the soft tissue collapsibility increases, the respiratory drive as well as arousal threshold decreases, and this condition predisposes to upper airway obstruction [33]. It has also been suggested that postmenopausal women who do not use hormone therapy have higher apneic thresholds than premenopausal females and hormone therapy users resulting in unstable breathing [32]. Of note, the increase in the occurrence of OSA was similar in both men and women after the age 50 years in the current cohort, suggesting the effect of aging per se as a contributing role on the increased collapsibility of the upper airways.

Another explanation for the higher age at OSA diagnosis in women could be that OSA is underrecognized due to atypical symtom presentations. Of note, the symptom burden of OSA was heavier in women though the OSA was less severe in terms of AHI. On the other hand, the categorization of the OSA severity based on the standard OSA metric, AHI, has been questionned during the last decade [28,30]. The new novel OSA metrics such as hypoxic burden, loop gain, arousal threshold, arousal intensity, delta heart rate might also be different in men and women, contributing to the different symptom manifestations. Indeed, endotypic analysis has shown that women have less upper airway collapsibility, better muscle compensation and lower respiratory arousal thresholds [34]. These features have been suggested to explain the relatively shorter durations of obstructive events in women, and more hypopnea events and fewer apnea events and less oxygen desaturation [35]. It has also been argued that women have later onset of OSA than men, but that they experience OSA at a time of quickly increasing cardiovascular risk factors [35].

One of the main explanations of the sex differences in the severity of OSA has been attributed to the increased predisposition to pharyngeal collapse in men. The fact that male airway is longer was proven by measurements from previous studies [20,36]. It has been suggested that men had increased pharyngeal airway length, increased soft palate area, and increased pharyngeal volume. However, no systematic differences were found in pharyngeal dilator muscle activation/responsiveness, or pharyngeal mechanics [20,36]. In a recent review, it has been suggested that sex-specific differences in the pathogenesis and presentation of OSA

reflect differences in responses to hypoxia and CO_2, as well as arousal threshold in addition to body fat distribution and upper airway anatomy [35].

Compared with men, women with OSA reportedly have more endothelial dysfunction and are more likely to develop hypertension and insulin resistance [37–40]. An increased incidence of left ventricular hypertrophy and heart failure were observed in aging women with moderate-to-severe OSA compared with women without OSA; disease incidence was partly explained by elevated plasma levels of high-sensitivity troponin (a marker of subclinical myocardial injury) [41]. Smoking, which causes endothelial dysfunction, seems to amplify the effect of OSA on the risk of incident cardiovascular disease, with the largest effects in women suggesting complex interactions between vascular disease risk factors, OSA and sex [42].

Regarding the polysomnography findings, our results confirm poor sleep quality in women in terms of less total sleep time, longer sleep latency and decreased deep sleep. Though not particularly addressed, these results are supportive for higher occurrence of comorbid insomnia in women than in men [43], which may have effect on adherence to PAP treatment.

The strengths of our study include the sample size of the study cohort, the structured questionnaires regarding symptoms, the gold standard polysomnographic investigations for the OSA diagnosis and the nationwide representatives of the study results.

We should also acknowledge certain limitations. Comorbidities were self-reported and a selection bias can therefore not be excluded. Snoring and witnessed apneas might be underreported among the patients without a bed-partner. The proportion of the participants from the cities and sleep centers were not equally distributed, so there might be some geographical differences between the regions. On the other hand, all sleep centers in the big cities such as Istanbul, Ankara, Izmir and Diyarbakır take care of patients from cities and rural areas and from different regions of the country, so we think that the distribution of the differences is representative nationwide. Similarly, the database does not include economic status of the participants and we can therefore not provide more detailed data between regions. Of note, there are other factors such as differences in health-related behaviors and access to care which may play role on the higher prevalence of comorbidities in women. These factors are not explored in the current manuscript. Finally, data regarding arousal index and periodic leg movements index were optional, and we had no complete data about those variables.

5. Conclusions

Our results suggest significant sex differences in sleep apnea severity, symptom presentations, and polysomnographic features in this large nationwide cohort. Women with OSA seem to have more symptom burden and comorbidities independent of age and obesity despite having a less severe OSA in terms of AHI compared to those findings in men. These aspects should be carefully considered in management of the individuals in order to avoid delay in diagnostic evaluation of OSA in women. Future studies would rely not only on AHI but also the novel parameters such as hypoxic burden, delta heart rate and arousal threshold, which hopefully might suggest how diagnosing OSA in women might benefit from a more holistic assessment.

CRediT authorship contribution statement

Aylin Pihtili: Writing – original draft, Investigation, Formal analysis, Data curation. **Esen Kiyan:** Writing – review & editing, Data curation. **Baran Balcan:** Writing – review & editing, Data curation. **Semih Arbatli:** Writing – review & editing, Data curation. **Aykut Cilli:** Writing – review & editing, Data curation. **Nejat Altintas:** Writing – review & editing, Data curation. **Aylin Özsancak Ugurlu:** Writing – review & editing, Data curation. **Canan Gündüz Gürkan:** Writing – review & editing, Data curation. **Mehmet Sezai Tasbakan:** Writing – review & editing, Data curation. **Nese Dursunoglu:** Writing – review & editing, Data curation. **Hamza Ogun:** Writing – review & editing, Data curation. **Ali Nihat Annakkaya:** Writing – review & editing, Data curation. **Sinem N. Sökücü:** Writing – review & editing, Data curation. **Hikmet Firat:** Writing – review & editing, Data curation, Conceptualization. **Özen K. Basoglu:** Writing – review & editing, Data curation, Conceptualization. **Yüksel Peker:** Writing – original draft, Validation, Supervision, Software, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Clinical trial registration

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Declaration of competing interest

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References

[1] Hnin K, Mukherjee S, Antic NA, Catcheside P, Chai-Coetzer CL, McEvoy D, et al. The impact of ethnicity on the prevalence and severity of obstructive sleep apnea. Sleep Med Rev 2018;41:78–86.
[2] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.
[3] Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019;7(8):687–98.
[4] Demir AU, Ardic S, Firat H, Karadeniz D, Aksu M, Uçar ZZ, et al. Prevalence of sleep disorders in the Turkish adult population epidemiology of sleep study. Sleep Biol Rhythm 2015;13:298–308.
[5] Bouloukaki I, Tsiligianni I, Schiza S. Evaluation of obstructive sleep apnea in female patients in primary care: time for improvement? Med Princ Pract 2021;30:508–14.
[6] Geer JH, Hilbert J. Gender issues in obstructive sleep apnea. Yale J Biol Med 2021;94(3):487–96.
[7] Zhang Z, Cheng J, Yang W, Zou H, Su C, Miao J. Gender differences in clinical manifestations and polysomnographic findings in Chinese patients with obstructive sleep apnea. Sleep Breath 2020;24(3):1019–26.
[8] Bonsignore MR, Saaresranta T, Riha RL. Sex differences in obstructive sleep apnoea. Eur Respir Rev 2019;28(154):190030.
[9] Lindberg E, Benediktsdottir B, Franklin KA, Holm M, Johannessen A, Jögi R, et al. Women with symptoms of sleep-disordered breathing are less likely to be diagnosed and treated for sleep apnea than men. Sleep Med 2017;35:17–22.
[10] Wimms A, Woehrle H, Ketheeswaran S, Ramanan D, Armitstead J. Obstructive sleep apnea in women: specific issues and interventions. BioMed Res Int 2016;2016:1764837.
[11] Basoglu OK, Tasbakan MS. Gender differences in clinical and polysomnographic features of obstructive sleep apnea: a clinical study of 2827 patients. Sleep Breath 2018;22(1):241–9.
[12] Bostan OC, Akcan B, Saydam CD, Tekin M, Dascı O, Balcan B. Impact of gender on symptoms and comorbidities in obstructive sleep apnea. Eurasian J Med 2021;53(1):34–9.
[13] Bock JM, Greenlund IM, Somers VK, Baker SE. Sex differences in neurovascular control: implications for obstructive sleep apnea. Int J Mol Sci 2023;24(17):13094.
[14] Gottlieb DJ, Punjabi NM. Diagnosis and management of obstructive sleep apnea: a review. JAMA 2020;323(14):1389–400.

[15] Yeghiazarians Y, Jneid H, Tietjens JR, Redline S, Brown DL, El-Sherif N, et al. Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American heart association. Circulation 2021;144(3):e56–67.
[16] Kapsimalis F, Kryger M. Gender and obstructive sleep apnea syndrome, part 1: clinical features. Sleep 2002;25(4):412–9.
[17] Hoffstein V, Szalai P. Predictive value of clinical features in diagnosing obstructive sleep apnea. Sleep 1993;16:118–22.
[18] Bixler E, Vgontzas A, Lin HM, Ten Have T, Rein J, Vela-Bueno A, et al. Prevalence of sleep disordered breathing in women. Effect of gender. Am J Respir Crit Care Med 2001;163:608–13.
[19] Tishler PV, Larkin EK, Schluchter MD, Redline S. Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. JAMA 2003;289(17):2230–7.
[20] Malhotra A, Huang Y, Fogel RB, Pillar G, Edwards JK, Kikinis R, et al. The male predisposition to pharyngeal collapse: importance of airway length. Am J Respir Crit Care Med 2002;166(10):1388–95.
[21] Kapsimalis F, Kryger MH. Gender and obstructive sleep apnea syndrome, part 2: mechanisms. Sleep 2002;25(5):499–506.
[22] Vagiakis E, Kapsimalis F, Lagogianni I, Perraki H, Minaritzoglou A, Alexandropoulou K, et al. Gender differences on polysomnographic findings in Greek subjects with obstructive sleep apnea syndrome. Sleep Med 2006;7(5):424–30.
[23] Huang T, Lin BM, Markt SC, Stampfer MJ, Laden F, Hu FB, et al. Sex differences in the associations of obstructive sleep apnoea with epidemiological factors. Eur Respir J 2018;51(3):1702421.
[24] O'Connor C, Thornley KS, Hanly PJ. Gender differences in the polysomnographic features of obstructive sleep apnea. Am J Respir Crit Care Med 2000;161(5):1465–72.
[25] Peker Y, Başoğlu ÖK, Fırat H, TURKAPNE Study Group. Rationale and design of the Turkish sleep apnea database - TURKAPNE: a national, multicenter, observational, prospective cohort study. Turk Thorac J 2018;19(3):136–40.
[26] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14(6):540–5.
[27] İzci B, Ardic S, Firat H, Sahin A, Altinors M, Karacan I. Reliability and validity studies of the Turkish version of the Epworth sleepiness scale. Sleep Breath 2008;12(2):161–8.
[28] American Academy of Sleep Medicine. International classification of sleep disorders. third ed. Darien, IL: American Academy of Sleep Medicine; 2014.
[29] Force AAoSMT. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22:667–89.
[30] Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med 2017;13(3):479–504.
[31] Young T, Finn L, Austin D, Peterson A. Menopausal status and sleep-disordered breathing in the Wisconsin sleep cohort study. Am J Respir Crit Care Med 2003;167:1181–5.
[32] Rowley JA, Zhou XS, Diamond MP, Badr MS. The determinants of the apnea threshold during NREM sleep in normal subjects. Sleep 2006;29:95–103.
[33] Saaresranta T, Aittokallio T, Polo-Kantola P, Helenius H, Polo O. Effect of medroxyprogesterone on inspiratory flow shapes during sleep in postmenopausal women. Respir Physiol Neurobiol 2003;134(2):131–43.
[34] Sands SA, Alex RM, Mann D, Vena D, Terrill PI, Gell LK, et al. Pathophysiology underlying demographic and obesity determinants of sleep apnea severity. Ann. Am. Thorac Soc 2023;20(3):440–9.
[35] Redline S, Azarbarzin A, Peker Y. Obstructive sleep apnoea heterogeneity and cardiovascular disease. Nat Rev Cardiol 2023;20(8):560–73.
[36] Sforza E, Bacon W, Weiss T, Thibault A, Petiau C, Krieger J. Upper airway collapsibility and cephalometric variables in patients with obstructive sleep apnea. Am J Respir Crit Care Med 2000;161:347–52.
[37] Faulx MD, Larkin EK, Hoit BD, Aylor JE, Wright AT, Redline S. Sex influences endothelial function in sleep-disordered breathing. Sleep 2004;27(6):1113–20.
[38] Korcarz CE, Stein JH, Peppard PE, Young TB, Barnet JH, Nieto FJ. Combined effects of sleep disordered breathing and metabolic syndrome on endothelial function: the Wisconsin Sleep Cohort study. Sleep 2014;37(10):1707–13.
[39] O'Connor GT, Caffo B, Newman AB, Quan SF, Rapoport DM, Redline S, et al. Prospective study of sleep-disordered breathing and hypertension: the sleep heart health study. Am J Respir Crit Care Med 2009;179(12):1159–64.
[40] Huang T, Sands SA, Stampfer MJ, Tworoger SS, Hu FB, Redline S. Insulin resistance, hyperglycemia, and risk of developing obstructive sleep apnea in men and women in the United States. Ann Am Thorac Soc 2022;19(10):1740–9.
[41] Roca GQ, Redline S, Claggett B, Bello N, Ballantyne CM, Solomon SD, et al. Sex-specific association of sleep apnea severity with subclinical myocardial injury, ventricular hypertrophy, and heart failure risk in a community-dwelling cohort: the atherosclerosis risk in communities-sleep heart health study. Circulation 2015;132(14):1329–37.
[42] Donovan LM, Feemster LC, Billings ME, Spece LJ, Griffith MF, Rise PJ, et al. Risk of cardiovascular disease related to smoking is greater among women with sleep-disordered breathing. J Clin Sleep Med 2018;14(11):1929–35.
[43] Mysliwiec V, Pruiksma KE, Matsangas P, Powell T, Straud CL, Taylor DJ, et al. STRONG STAR Consortium. Sex differences in US military personnel with insomnia, obstructive sleep apnea, or comorbid insomnia and obstructive sleep apnea. J Clin Sleep Med 2024;20(1):17–30.