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RESEARCH

CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND OBSTRUCTIVE SLEEP APNEA SYMPTOMS: AN OUTPATIENT-BASED POPULATION STUDY IN TURKEY

ABSTRACT

Introduction: This study aimed to assess the factors associated with the coexistence of COPD and OSA symptoms.

Materials and Method: An interviewer-administered questionnaire and pulmonary function testing was applied to 2199 (female: 52.2%) subjects, admitted to the outpatient clinics of chest medicine in a Training and Research Hospital in Ankara. COPD was defined as the FEV1/FVC of <0.7. OSA symptoms was defined as the presence of all three symptoms snoring, witnessed apnea and daytime sleepiness.

Results: Prevalence of COPD, OSA symptoms and coexistence of COPD and OSA symptoms were 29.4, 4.0, 2.2 in men and 11.6, 5.0, 0.5 in women, respectively. There was a strong association between age, male gender, ever exposure to fume, family atopy, lower education status and coexistence of COPD and OSA symptoms after the adjustment for age, gender, BMI and pack-year of smoking. Among males, FEV1% was lower in the COPD coexistence group than COPD only group (beta; 95%CI: -7.6; -0.4 to -14.8) after the adjustment for pack year of smoking.

Conclusion: Atopic status and fume exposure could be risk factors for OSA in COPD patients. This association should be evaluated in further, follow-up studies with the confirmation of OSA diagnosis.

Key Words: Pulmonary Disease, Chronic Obstructive; Sleep Apnea, Obstructive; Risk Factors.

ARAŞTIRMA

KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞI VE OBSTRÜKTİF UYKU APNE SEMPTOMLARI: TÜRKİYE'DEN HASTANE TEMELLİ BİR ÇALIŞMA

ÖZ

Giriş: Kronik obstrüktif akciğer hastalığı (KOAH) ve obstrüktif uyku apne sendromu bağlantılı olmamalarına karşın birlikte görülebilir ve kardiyovasküler komplikasyon için risk oluşturabilirler. KOAH ve OSA birlikteliği ile ilgili bilgiler sınırlıdır. Çalışma KOAH ve OSA semptomlarının birlikteliği ile ilişkil etkenleri incelemek amacıyla yapıldı.

Gereç ve Yöntem: Görüşmeci tarafından uygulanan soru formu ve solunum fonksiyon testi Ankara'da bir eğitim araştırma hastanesi göğüs hastalıkları polikliniğine başvuran 2199 kişiye (kadın: %52.2) uygulandı. KOAH FEV1/FVC <0.7 olarak tanımlandı. OSA semptomları horlama, tanıklı apne ve güniçi uykululuk semptomlarının her üçünün olmasıyla tanımlandı.

Bulgular: Prevalanslar KOAH, OSA ve KOAH ve OSA semptomlarının birlikteliği için erkeklerde %29.4, %4.0 ve %2.2, kadınlarda %11.6, %5.0 ve %0.5 idi. Yaş, cinsiyet, beden kitle indeksi, paket-yıl sigara içimi ile uygunlaştırıldıktan sonra KOAH ve OSA semptomlarının birlikteliği yaş, erkek cinsiyet, duman maruziyeti, ailesel atopi, düşük eğitim düzeyi ile ilişkili bullundu. Erkeklerde FEV1%'si KOAH ve OSA semptomlarının birlikteliği paket-yıl sigara içimi ile uygunlaştırıldıktan sonra sadece KOAH olan gruptan düşük bulundu (beta; 95%GA: -7.6; -0.4 ile -14.8 arası).

Sonuç: Atopik durum ve duman maruziyeti KOAH'da OSA riski ile ilişkili olabilir. Bu ilişki sonraki yapılacak ve OSA tanısını kesinleştiren izlem çalışmalarında değerlendirilmelidir.

Anahtar Sözcükler: Kronik Obstrüktif Akciğer Hastalığı; Obstrüktif Uyku Apnesi; Risk Faktörleri.

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a common disorder characterized by recurrent upper airway collapse during sleep with the consequences of poor sleep quality, sympathetic overdrive and hypoxemia (1). The prevalence of OSAS in the adult population varies from 2% to 4% in studies from different parts of the world (1). Discrepancies in the prevalence are partly due to differences in the populations studied and non-standardized definitions and diagnostic methods used in different studies (1).

Chronic obstructive pulmonary disease (COPD) is a condition of progressive deterioration of the respiratory system characterized by obstruction of pulmonary airways and decreased airflow (2). Prevalence of COPD, defined by an FEV1/FVC ratio less than 0.7 (GOLD stages I–IV) is above 10% in adults 40 years of age or older, and may exceed 20% (2-4). Complaints related to unrestorative sleep has frequently been reported in COPD patients, which included objective evidence of reduced sleep efficiency, delayed sleep onset, reduced total sleep time and frequent periods of wakefulness (5). Causes of poor-quality sleep in COPD are probably multifactorial and include nocturnal cough, nocturnal dyspnea, use of drugs such as theophylline and the effects of aging on sleep (5). Though there is no causal link, OSAS sometimes coexists with COPD and this combination is called as "overlap syndrome" (5).

The main goal of this study was to assess the risk factors for the coexistence of COPD and OSA symptoms.

MATERIALS AND METHOD

Participants were recruited from the outpatient Chest Medicine Clinic in a training and research hospital in Ankara. Participants providing consent were asked to fill an interviewer-administered questionnaire, including 35 questions on symptoms of chronic respiratory diseases and OSAS, personal characteristics, dietary habits, environmental and occupational factors. In the repeated administration of the test to a group of subjects (n: 30), test retest repeatability for the questions on COPD and OSA symptoms was perfect (Cohen's Kappa: 1.0).

A nurse recorded the participants' weight and height. Body mass index (BMI) was calculated by dividing the weight (kg) to square of height (m). Spirometer (Sensormedics) was used to measure the forced vital capacity (FVC), and forced expiratory volume in one second (FEV1), as the patient was seated. Best of the three maneuvers was recorded. Predicted values of pulmonary function testing based on height and age, as adopted by Knudson et al., were used to calculate the percentage of the predicted FEV1 and FVC (6,7).

COPD was defined according to the criteria of GOLD as in the following (2):

i. any of the symptoms of dyspnea, chronic cough, chronic sputum and,
ii. FEV1/FVC < 0.7 and,
iii. FEV1 unresponsive to bronchodilators (after the administration of 400 mcg albuterol increase in FEV1 < 200 ml and <12%).

FEV1 % of predicted (denoted as FEV1% in the text and tables) was used to assess the severity of COPD.

OSA symptoms were defined by the presence of all three symptoms of snoring, witnessed apnea and daytime sleepiness. Daytime sleepiness was assessed by responding 'yes' to both of the questions which were about feeling sleepy and the possibility of falling asleep during the day.

Patients were classified into four groups as normal, COPD only, OSA symptoms and coexistence of COPD and OSA symptoms. COPD only group did not have OSA symptoms. Normal group had normal pulmonary function testing results and did not have OSA symptoms.

Subjects with OSA symptoms were invited to the sleep laboratory for overnight polysomnography (PSG) examination. Diagnosis of OSAS was determined by standard overnight polysomnography (16 channels, Embla, Flaga) for apnea-hypopnea index (AHI) of 5/h or more and excessive daytime sleepiness or AHI ≥ 15/h (8).

All the participants singed written informed consent. The study complied with the Declaration of Helsinki and was approved by the local research ethics committee.

Statistical Analysis

Prevalence % of COPD and OSA symptoms was tabulated separately for men and women in the study. Comparisons were made between the exclusive disease groups of OSA symptoms, COPD and coexistence of COPD and OSA. Subjects without any of the diseases (normal group) were considered as the reference group. Mean and standard deviation (SD) of the continuous data were reported. Each disease group was compared with the normal group. Univariate association between disease groups and demographics and personal characteristic of the subjects was investigated by Chi-square testing and independent samples t-test for categorical and continuous variables, respectively. One-way ANOVA test with

Dunnett's test (comparison of the groups with the normal group) was used for multiple comparison of the continuous variables. Independent association between disease groups and explanatory factors was assessed via logistic regression analysis models, after the adjustment for age, gender and relevant risk factors. Multiple linear regression analysis was used to adjust for the association between the disease groups and pulmonary function testing results. Relative risk estimates (OR's for logistic regression analysis) and regression coefficients (beta regression coefficient for linear regression analysis) with 95% confidence intervals of these estimates were presented. P value less than 0.05 was selected for statistical significance, and values < 0.01 and < 0.001 were also marked. SPSS software (version 11.0) was used in the data analysis.

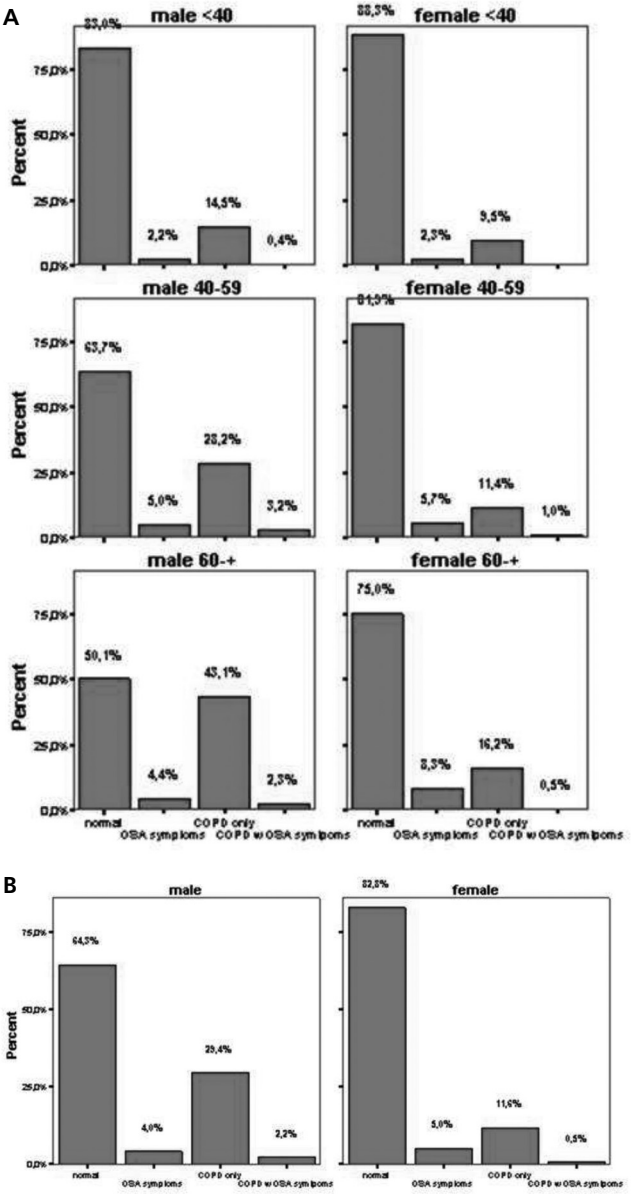

Figure 1— Prevalence percentage of exclusive diseases by gender A: in different age groups, B: in total (COPD: chronic obstructive pulmonary disease, OSA: obstructive sleep apnea, w: with).

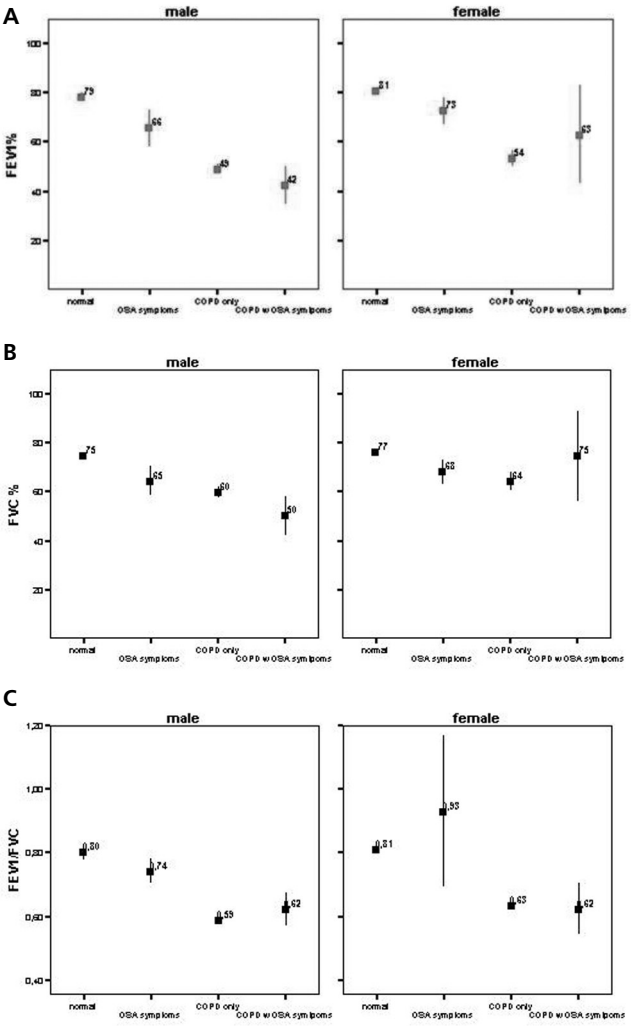

Figure 2— Pulmonary function testing results of the subjects according to exclusive disease groups by gender. Bars represent the mean and the 95% CI's. A: FEV1%, B: FVC%, C: FEV1/FVC (COPD: chronic obstructive pulmonary disease, FEV1%: predicted % of forced expiratory volume at one second, FVC%: predicted % of forced vital capacity, FEV1/FVC: FEV1 divided by FVC, OSA: obstructive sleep apnea, w: with).

RESULTS

Of the 2199 subjects 1062 were men and 1137 were women. Figure 1 shows the distribution of diseases by age and gender. Percentage of COPD, OSA symptoms, and coexistence of COPD and OSA symptoms were 29.4, 4.0, 2.2 in men and 11.6, 5.0, 0.5 in women, respectively. Prevalence of the diseases were higher in the older age groups. In the age groups of 50 years -59 years and 60 years-above, prevalence percentages of the diseases were significantly different between men and women.

Pulmonary function testing results of the subjects by gender in exclusive disease groups is shown in Figure 2. In men and women all disease groups had significantly lower FEV1% and FVC% than the control group.

Associations between disease groups and potential risk factors for male and female subjects are shown in Table 1 and 2, respectively. Among men, OSA symptoms group had higher BMI than normal group; COPD group was significantly associated with respiratory infections during childhood, regular alcohol ingestion in the past, ever dust exposure at work, and smoking. Both COPD and coexistence of COPD and OSA symptoms groups were significantly associated with family atopy and lower educational level. COPD and OSA symptoms groups were associated with dietary intake of unsaturated fatty acids in the past. Among women, OSA symptoms group had higher BMI than normal group; COPD group was significantly associated with respiratory infections during the childhood, lower educational level and dung expo-

Table 1— Univariate Association Between Exclusive Disease Groups and Characteristics of the Male Subjects

	Normal	COPD Only	OSA Symptoms	Coexistence of COPD and OSA Symptoms	Total
Age (yr) mean (SD)	47.4 (15.1)	65.4 (13.3)§	53.7 (12.5)*	56.4 (9.7)*	50.7 (15.0)
BMI, (kg/m^2) mean (SD)	26.1 (4.4)	25.5 (3.6)	29.3 (5.4)§	27.6 (5.5)	26.2 (4.4)
Family atopy	21.3	31.8*	33.3	47.4*	25.0
Respiratory infection in the childhood	39.8	67.7§	46.7	52.6	46.7
Dung exposure	38.0	46.0	53.3	57.9	40.3
Education Status					
No school	6.9	16.7§	16.7	36.8§	9.4
Primary	71.3	71.7	56.7	63.2	71.1
Higher school	21.8	11.6	26.7	–	19.4
Alcohol intake	40.3	54.5§	43.3	31.6	43.5
Dietary intake of unsaturated fatty acids	64.3	53.5*	36.7*	36.8	60.9
Work Exposure					
Ever dust	55.4	73.7§	56.7	73.7	60.0
Ever fume	23.3	29.3	26.7	47.4	25.2
Smoking Status					
Never smoked	20.3	14.6§	13.3	15.8	19.2
Ex-smoker	48.4	64.6	60.0	57.9	51.9
Current smoker	31.3	20.7	26.7	26.3	28.9
Pack-year of smoking mean (SD)	18.5 (18.4)	30.0 (23.8)§	23.4 (21.0)	26.6 (18.8)	20.8 (20.0)
Nocturnal Symptoms					
Cough	42.1	63.1§	50.0	84.2§	49.2
Shortness of breath	34.4	61.6§	73.3§	84.2§	43.6

BMI: body mass index, COPD: chronic obstructive pulmonary disease, OSA: obstructive sleep apnea, yr: years.
COPD only: COPD patients who do not have coexisting OSA symptoms as defined in the Methods.
Percentages are provided in the Table, unless otherwise specified.
Comparisons were made between disease groups and the normal group.
*p<0.05, †p<0.01, §p<0.001
Significant findings are marked in bold type.

Table 2— Univariate Association Between Exclusive Disease Groups and Characteristics of the Female Subjects

	Normal	COPD Only	OSA Symptoms	Coexistence of COPD and OSA Symptoms	Total
Age (yr) mean (SD)	44.7 (14.2)	48.4 (14.8)*	52.2 (12.1)†	52.3 (12.4)	45.5 (14.3)
BMI, (kg/m²) mean (SD)	28.7 (6.0)	28.3 (4.8)	33.1 (7.0)§	33.5 (3.3)	28.9 (6.1)
Family atopy	27.7	38.3	52.9§	75.0	29.8
Respiratory infection in the childhood	42.5	64.2§	54.9	25.0	54.3
Dung exposure	37.0	51.9*	54.9	50.0	40.1
Education Status					
No school	25.6	48.1§	49.0	50.0	28.6
Primary	56.8	44.4	49.0	50.0	55.2
Higher school	17.6	7.4	2.0	–	16.2
Alcohol intake	2.7	2.5	–	–	2.7
Dietary intake of unsaturated fatty acids	68.9	59.3	56.9	75.0	67.4
Work Exposure					
Ever dust	28.5	38.3	47.1*	50.0	31.2
Ever fume	2.6	4.9	7.8	–	3.1
Smoking Status					
Never smoked	68.2	81.5	70.6	75.0	68.7
Ex-smoker	13.6	14.8	7.8	25.0	13.7
Current smoker	18.2	3.7	21.6	–	17.6
Pack-year of smoking mean (SD)	3.5 (8.3)	3.5 (12.6)	5.3 (11.1)	0.6 (1.1)	3.8 (1.1)
Nocturnal Symptoms					
Cough	58.3	76.5†	76.5*	100.0	61.6
Shortness of breath	41.9	67.9§	86.3§	100.0	47.4

BMI: body mass index, COPD: chronic obstructive pulmonary disease, OSA: obstructive sleep apnea, yr: years.
Percentages are provided in the Table, unless otherwise specified.
Comparisons were made between disease groups and the normal group.
*p<0.05, †p<0.01, §p<0.001
Significant findings are marked in bold type.

sure. OSA symptoms group was significantly associated with family atopy and ever exposure to dust at work.

Factors, associated with the disease groups were investigated in the logistic regression analysis models, as shown in Table 3. In these models the association of each factor with COPD group was adjusted for age, gender and pack-year of smoking; with OSA symptoms group for age, gender and BMI; and with coexistence of COPD and OSA symptoms group for age, gender, BMI and pack-year of smoking. Both COPD and coexistence of COPD and OSA symptoms groups were significantly associated with female gender (OR=0.5, 95%CI=0.3-0.7 for COPD, OR=0.17, 95%CI=005-0.59 for coexistence of COPD and OSA symptoms); with age (OR=1.04, 95%CI=1.03-1.05 for COPD, OR=1.04, 95%CI=1.00-1.07 for coexistence of COPD and OSA symptoms), family atopy (OR=1.6, 95%CI=1.2-2.1 for COPD, OR=3.6, 95%CI=1.6-8.3 for coexistence of COPD and OSA symptoms), and lower educational level (OR=1.5, 95%CI=1.1-2.2 for COPD, OR=5.2, 95%CI=1.9-13.9 for coexistence of COPD and OSA symptoms). In addition to these, COPD group was significantly associated with BMI (OR=0.94, 95%CI=0.91-0.97), respiratory infection in the childhood (OR=2.7, 95%CI=2.0-3.6) and exposure to dust (OR=1.6, 95%CI=1.2-2.2); coexistence of COPD and OSA symptoms group was significantly associated with fume exposure (OR=2.7, 95%CI=1.1-6.6). OSA symptoms group was significantly associated with age (OR=1.02, 95%CI=1.00-1.04), BMI (OR=1.10, 95%CI=1.06-1.14), family atopy (OR=2.4, 95%CI=1.5-3.8), dung exposure (OR=1.6, 95%CI=1.0-2.6) and lower educational level (OR=2.0, 95%CI=1.1-3.6).

In the analysis of pulmonary function testing with multiple linear regression analysis, among men, coexistence of COPD and OSA symptoms group had lower FEV1 % than

Table 3— Adjusted Association Between Exclusive Disease Groups and Potential Risk Factors

	COPD only OR (95% CI)	OSA symptoms OR (95% CI)	Coexistence of COPD and OSA symptoms OR (95% CI)
Gender, female	0.5 (0.3-0.7)§	1.0 (0.6-1.6)	0.17 (0.05-0.59)†
Age (yr)/1 year increase	1.04 (1.03-1.05)§	1.02 (1.00-1.04)†	1.04 (1.00-1.07)*
BMI (kg/m²)/1 kg/m² increase	0.94 (0.91-0.97)§	1.10 (1.06-1.14)§	1.06 (0.98-1.16)
Pack-year of smoking /1 pack-year increase	1.01 (1.04-1.01)†	1.01 (0.99-1.02)	1.00 (0.98-1.02)
Family atopy	1.6 (1.2-2.1)§	2.4(1.5-3.8)§	3.6 (1.6-8.3)†
Respiratory infection in the childhood	2.7 (2.0-3.6)§	1.4 (0.9-2.2)	1.8 (0.8-4.1)
Dung exposure	1.2 (0.9-1.5)	1.6 (1.0-2.6)*	1.7 (0.7-4.0)
Not completed primary school	1.5 (1.1-2.2)	2.0 (1.1-3.6)*	5.2 (1.9-13.9)§
Ever exposed to dust	1.6 (1.2-2.2)§	1.4 (0.9-2.3)	1.9 (0.8-4.8)
Ever exposed to fume	1.3 (0.9-1.9)	1.5 (0.8-3.0)	2.7 (1.1-6.6)*

BMI: body mass index, COPD: chronic obstructive pulmonary disease, OSA: obstructive sleep apnea, yr: years.
Logistic regression models were constructed separately for each disease group.
Normal group was defined as the reference group.
Models adjusted for age, gender and pack-year of smoking in COPD; age, gender and BMI in OSA symptoms; age, gender, BMI and pack-year of smoking in coexistence of COPD and OSA symptoms.
*p<0.05, †p<0.01, §p<0.001
Significant findings are marked in bold type.

COPD group after the adjustment for pack-year of smoking (beta coefficient=-7.6, 95% CI=-0.4 to -14.8, results not shown).

All subjects with OSA symptoms were invited for overnight PSG examination. Of these subjects, 82% did not want to attend to the sleep lab for PSG examination (73% did not want to spend one night at the hospital for the examination and 9% were scheduled but did not come). In the 23 tested subjects (4 females, 19 males), OSAS was confirmed in 14 (60.9 %). Subjects who attended PSG had higher BMI, lower proportion of women and higher proportion of smokers than that of the subjects, who did not attend to the sleep lab.

DISCUSSION

This cross sectional study provided information on the prevalence of OSA symptoms in the COPD patients. Despite its weaknesses, it helped to generate hypotheses about the risk factors of the coexistence of COPD and OSA.

OSA Symptoms and Associated Factors

Scanty data exists about the prevalence of OSA in Turkey. In a community based survey of 5339 persons aged 20-107 years in a city from the central region of Turkey, the prevalence of insomnia, habitual snoring, obstructive sleep apnea and daytime hypersomnolence was 40.3%, 37.0%, 6.4%, 24.0% respectively (9). In this study, prevalence of OSA symptoms was found as ~3-4 %. Surprisingly, prevalence of OSA symptoms in female subjects was higher than the male subjects, presumably due to higher prevalence of obesity in the female than the male participants, which is a major risk factor for OSAS (10).

In this study, OSA symptoms were defined by the presence of all three symptoms of snoring, witnessed apnea and daytime sleepiness. In a primary care setting, three criteria for high risk of sleep apnea included snoring, persistent daytime sleepiness or drowsiness while driving, and obesity or hypertension (1). In a series of consecutive overweight patients, presence of three or more of the four features (habitual snoring, interrupted nocturnal breathing as reported by the spouse or roommates, excessive daytime sleepiness, and arterial hypertension) had a sensitivity and specificity of 80% and 45%, respectively (11). Laboratory testing confirmed OSAS in ~60% of the OSA symptoms group in this study. This makes interpretation of our findings related to the prevalence of OSA difficult. We think that our findings on the association between OSA symptoms and diseases are meaningful for relating the clinical symptoms and should be tested in further studies.

This study revealed a very strong association with OSA symptoms and BMI as found in previous studies (12,13). Other associated factors were family atopy, lower educational

level and dung exposure. In a study from outpatient clinics in Switzerland of 72 OSAS patients and 44 COPD patients, OSAS patients were more likely to be sensitized to perennial allergens and have symptoms of perennial allergic rhinitis than patients with COPD (14). Perennial allergens and particularly perennial allergic rhinitis might be a risk factor for OSA via increasing nasal airway resistance (15). Lower educational level is known to be related with poor self-perceived health and obesity (16). Other factors related to lower education level including poor oral hygiene and frequent respiratory infections could also be a risk factor for OSA.

COPD and Associated Factors

In Turkey, COPD is the third major cause of death and sixth most prevalent disease (17). A recently published prevalence study revealed the prevalence of COPD in Turkey as 6.9%, ranging from 18.1% in current smokers over 40 years of age to 4.5% among younger smokers (18). Prevalence of COPD in our study was 29.4% in male and 11.6% in female subjects. Since the study population included patients admitted to the department of chest diseases with a smoking rate of ~80%, prevalence of COPD in this study is likely to be an overestimate. In our study, smoking, respiratory infections during childhood, work related exposure to dust and family atopy were strongly associated with COPD. Occupational dust exposure has been shown as a risk factor for COPD (19). Previous studies have shown that use of dung for heating and cooking purposes (biomass exposure) in rural parts of the Turkey is an important risk factor for COPD in non-smoking women (18, 20). Respiratory infections during childhood and atopy were suggested as risk factors in developing COPD (4). Lower BMI in COPD, which is a risk factor for mortality in COPD, indicates the severity of COPD in this study (4). Thus our findings are consistent with the previous studies.

Coexistence of COPD and OSA Symptoms

Quality of sleep in COPD is likely to be influenced by the presence of sleep apnea syndrome, but not by the severity of airway obstruction (21). Severe obstructive airway disease was associated with worse sleep disordered breathing during REM sleep (22). In our study among men, coexistence of COPD and OSA symptoms group had a lower FEV1 % than COPD group after the adjustment for pack-year of smoking.

Chaouat et al. investigated the association of chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea syndrome, and found older age, lower FEV1%, and FEV1/FVC in the overlap syndrome group than the OSAS group, and reported lower FEV1% and lower FEV1/FVC in the overlap syndrome group (23) than that of the Sleep Heart Health Study, which was population based (21). In our study, COPD patients with OSA symptoms had lower BMI (27.6 kg/m^2 and 30.5 kg/m^2-36 kg/m^2, respectively) and lower FEV1% (36.2% and 52%-63%, respectively), than that of COPD patients with OSA diagnosis in the previous studies (23-25). These findings suggest that our study included a higher proportion of severe COPD patients.

Association (least a causal association) between COPD and OSA has not been shown and the occurrence of the two diseases together could be due to chance in almost 10% of the COPD cases (5). The proportion of OSA in COPD was 13% (range: 7% to 11% in different age groups) in male, and 39% (range: 34% to 43% in different age groups) in female COPD patients in our study. Higher risk of coexistence of COPD and OSA symptoms in men than women is similar to the status for COPD. This gender difference should be investigated in further studies including PSG testing.

Factors associated with the coexistence of COPD and OSA symptoms were lower educational status and fume exposure after the adjustment for age, gender and BMI. Lower educational status was associated with both COPD and OSA symptoms. A case control study has shown the association between COPD and exposure to fume in the past (26). As relates to the association of OSA symptoms with dung exposure, such exposure could be increasing the risk of OSA due to its influence on upper airway.

Limitations of the Study

A major limitation of the study was due to the study population, which was outpatient-based. However the study hospital was the largest social security hospital, which served for the population mainly among the workers and their family members (~ 42 million of the 76 million general population, as for the time of the study). Though hospital based, our study population had features representative of the general population. This should be considered in the interpretation of study results. Another major limitation was the lack of an objective assessment of OSA. Low attendance rate for PSG precluded the assessment of the validity of the study definition of OSA.

Reliability of the questionnaire used in the study was found appropriate in the testing retesting of 30 patients. However, validity of the information obtained from the subjects' reporting is still doubtful. The study was not focused on sleep symptoms. Since subjects with OSA or COPD are not different in the likelihood of reporting these symptoms than

the normal group, this would not bias the associations found in the study. Sleep problems in COPD patients might have been overreported due to the severity of disease and might be misclassified as OSA symptoms. Though FEV% of male patients was lower in coexistence of COPD and OSA symptoms group than COPD only group, this could also be due to more severe disease in the coexistence group.

Due to cross-sectional design, data about the consequences of the diseases like respiratory failure and pulmonary hypertension is missing. Causality interpretation of our findings is difficult due to cross-sectional design. However, our findings provide hypotheses, which should be tested in prospective studies. The main strength of this study is the investigation of COPD and related factors by standard pulmonary function testing in a large sample of adults in both genders, which likely represent the general population.

In conclusion prevalence of OSA symptoms in the middle-aged population was found as 4.3% in males and 4.9% in females in this outpatient based population study. Prevalence of COPD was 18.6% in males and 7.1% females. There was a strong association between BMI and OSA symptoms. For COPD, smoking and respiratory infections during childhood were the potential risk factors. Family atopy and fume exposure were strongly associated with coexistence of COPD and OSA symptoms. These associations should be evaluated in further studies with PSG confirmation of coexistence of COPD and OSA.

Conflict of Interest

The authors did not declare any conflict of interest related to the investigation and production of the manuscript.

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