Etiology of COPD in Non-Smoker Females

SİGARA İÇMEYEN KADINLARDA KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞININ ETİYOLOJİSİ

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Summary

Thirty women with Chronic Obstructive Pulmonary Disease (COPD) were included in the study aimed to find out the etiologic risk factors. A11 of them were non-smokers. The mean age of patients was 64.17 (47-85). The mean duration of disease period was 14.23 years. Out of 30, 22 patients were house -wife, two patients dealt with cleaning (retired of work), one was teacher (retired of work), one was a house -wife who dealt with coal delivery in the city 20 years ago for 5 years. Two were civil- servants (retired) and one was a nurse (a mid-wife- retired of work).

The number of patients who have been living in the city for all their -lives, who have been in rural area all life long and, who have been to both area were 10 (33%), 8 (26%) and 12 (40%), respectively. Biomass exposure has been noted in 12 (40%) patients with the mean duration of disease was 38.30 years (9-66). The statistical relationship between COPD and biomass exposure is significant ($p<0.06$). The history of frequent infections was present only in one patient where as there has been no history of bronchial asthma in any of the patients. The history of past lower respiratory tract infection was presented in 5 (16,6%) patients without any sequala. The family history of COPD was present in 15 (50%) patients. In 4 (13%) patients, the level of a) - antitrypsin in serum has been found lower than the normal range of 140-320 mg/dl (137.8 mg/dl, 137.8 mg/dl, 127 mg/dl). So it has been firstly concluded that it's necessary to search for a] - antitrypsin deficiency in the serum of nonsmoker-female patients with COPD. And secondly the passive cigarette-smoke exposure and biomass exposure are the most important risk factors. Lastly it's also worth paying attention for the indoor- airpollution in the development of COPD.

Key Words: COPD, Female patients, Etiology

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Özet

Sigara içmeyen 30 KOAH'lı kadın hastada etyolojik risk faktörleri araştırıldı. Hastaların yaş ortalaması 64.17 (47-85) olup, ortalama hastalık süresi 14.23 olarak bulundu. Hastaların 22'si evhanımı, 2'si emekli temizlik işçisi, l'i emekli öğretmen, I'i evhanımı ancak 20 yıl önce 5 yıl süreyle kömür nakliye işiyle uğraşmış, 2'si emekli hizmetli, l'i emekli hemşire, l'i çiftçi idi.

Sürekli şehirde yaşamış hasta sayısı 10 (33%), köyde yaşamış hasta sayısı 8 (26%), hem köyde, hemde şehirde yaşamış hasta sayısı ise 12 (%40) olarak saptandı. Hastaların 2 l'inde (%70) pasif sigara içiciliği vardı. Biomass maruziyet süresi ortalama 38.30 (9-66) yıl idi. Sık enfeksiyon öyküsü 1 hastada varken, hiçbir hastada bronşial astma öyküsü yoktu. Geçirilmiş alt solunum yolu enfeksiyonu 5 (%16.6) hastada vardı, ancak hiçbirinde sekel gözlenmedi.

Ailede KOAH öyküsü 15 (%50) hastada saptandı. Hastaların 4'ünde (%13) *a*\ -antitripsin düzeyi düşük olarak bulundu (137.8 mg/dl, 137.8 mg/dl, 132.1 mg/dl, 127.5 mg/dl-normal değerler: 140-340 mg/dl).

Sonuç olarak çalışmamızda öncelikle düşük a]-antitripsin, daha sonra pasif sigara içimi ve biomass maruziyeti önemli risk faktörleri olarak bulunmuştur. Ayrıca, hastalığın ortaya çıkmasında ev içi hava kirliliğinin önemli olması dikkat çekicidir.

Anahtar Kelimeler: KOAH, Kadın, Etyoloji

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Chronic Obstructive Pulmonary Disease (COPD) is a clinical picture characterized by progressive airway obstruction due to chronic bronchitis or emphysema. It may be together with airway hyperreactivity which might be partially reversible (1).

Nowadays both mortality and morbidity due to COPD show a tendency to increase.The increase in

morbidity changes among countries due to differences in genetic, ethnic, socioeconomic, occupational and environmental factors. In Turkey this value was 141,5 per hundred-thousand in 1992 (2). Although it hasn't been calculated definitely, for the statistical group into which the number of cases with brochial asthma has been included, only the cases died in the hospital were represented in the Annuals of Hospital Statistics. According to the data given in the Annual of 1992, 1086 patients died due to chronic bronchitis or emphysema or bronchial asthma..The mortality ratio was 1854 per hundred-thousand.

Again, in the same year, 20% of pulmonary disease patients died after hospitalisation due to COPD and bronchial asthma (2).

It's important to know the etiologic factors of COPD in taking some precautions against its development. Smoking is the most important etiologic risk factor in terms of mortality and morbidity (3). Environmental and personal risk factors other than smoking have a minor role in the etiology of COPD. However, it's also important to clarify these factors in order to make diagnosis and treatment satisfactorily. From this point of view we included 30 female patients over 45 years of age diagnosed according to American Thoracic Society.

Materials and Methods

We studied on randomized selected 30 non-smoker female patients with COPD between November 1998 and March 1999 at Atatiirk Medical Center of Respiratory Diseases and Thoracic Surgery (Ankara), Ankara Numune Hospital and Clinics of Respiratory Diseases at Ankara University, Faculty of Medicine. They have been diagnosed according to the criteria of American Thoracic Society. To distinguish COPD from asthma skin pric test was used, total Ig E, blood eosinophil count and marked decline pulmonary function tests, decrease in reversibility of obstruction following administration of inhaler bronchodilatators. None of the patients had atopy history.

We evaluated our study group by means of history of occupation, place and duration of living, biomass-exposure, passive-cigarette smoke exposure, and its duration, past respiratory infection, alcohol-intake, past frequent infections other than respiratory ones, routine laboratory studies (CBC, biochemical assays, etc), respiratory studies (chest -x ray film, tests of pulmonary functions) and measurement of serum a!-antitrypsin (AAT) level has been made by using turbidimetric and nephelometric methods by means of PAKO-Rabbit Antihuman ^-antitrypsin Code No Q 0363 Serum at the normal range of 140-320 mg/dl. >

Results

The patients were all female with the mean age of 64,17 years. In Table 1 the occupational status is shown.

When we examine place of living, the number of patients who have been living in urban for all their lives, who have been in rural and who have been to both areas are 10 (33%), 8 (26%) and 12 *(40%),* respectively (Table 2).

We have determined biomass exposure in 12 (40%) patients. The statistical relationship between COPD and biomass exposure is significant (p<0,06). The mean duration of biomass exposure is 38.30 years (the shortest 9 years, the longest 66 years).

Table 1. The occupational status of the study group.

Occupations	Number of patiens
Housewife	22
Teacher *	1
Nurse* O	1
Civil- servant*	2
Transporter(coal- delivery woman) ©	1
Cleaning worker**	2
Farmer	1
Total	30

*Retired of work oServant at school OTwenty years ago for five years,and also a housewife OA midwife.

Table 2. The distribution of cases according to place of living

Place of living	Number of cases	Percentage(%)
Urban	10	33
Rural	8	26
Urban+Rural	12	40

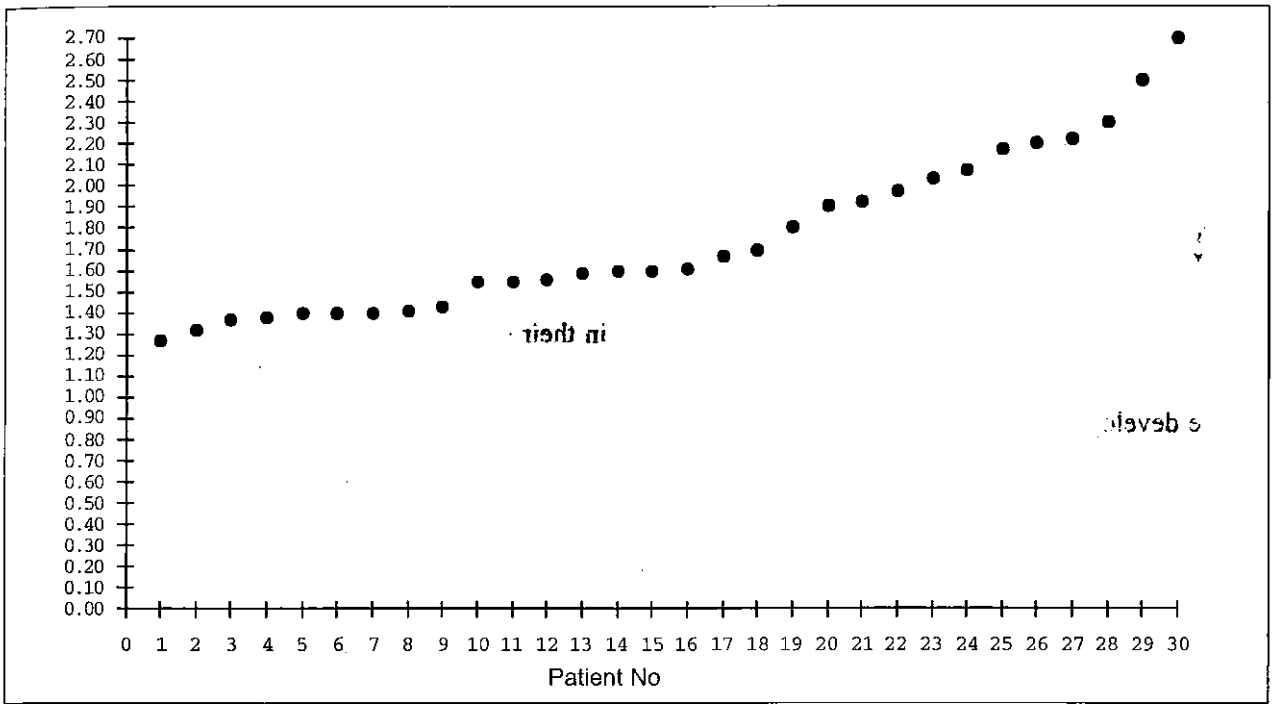

Figure 1. ai-antitrypsin levels of patients.

No history of alcoholic beverage intake has been found in any of our patients. We have found out the history of past-lower respiratory tract infections in 5 (16,6%) patients, and frequent respiratory tract infections only in 1 (3,3%) patient. There has been no sequala in any of the patients. And also there has been the family history of COPD in 15 (50%) patients. We have found serum a[-antitrypsin levels low in 4 (13%) patients (137.8 dm/dl, 137.8 mg/dl, 132.1 mg/dl, 127.5 mg/dl), a value which is statistically insignificant (p=0,05) (Figure 1).

Discussion

COPD is a disease characterized by air -way obstruction due to chronic bronchitis or emphysema according to the criteria of American Thoracic Society. Airway-obstruction is generally progressive. It might be together with airway -hyperreactivity and partially reversible. Chronic bronchitis is together with chronic productive coughing which lasts 3 months a year in two consecutive years without any other reason.

Emphysema is an abnormal dilatation of airways beyond terminal bronchioli due to destruction of bronchiolar walls without prominent fibrosis. This dilation stays permanently (1).

There are some definitive risk factors of development of COPD as smoking, a]-antitrypsin (AAT) deficiency, occupational exposure to dust and fumes.

Other possible risk-factors of COPD are air-pollution, low socioeconomic status, alcohol intake, passive exposure to smoking during childhood, low-birthweight, respiratory infections during childhood, atopy, bronchial hyperreactivity and familial tendency to develop COPD (4).

In this study we aimed to clarify the etiologic factors of COPD in females who have never smoked cigarette and haven't been exposed to chemical gases, fumes and dusts during their occupation. We searched for 30-nonsmoker female patients with COPD aged over 45 years and measured serum AAT levels and made routine laboratory tests (CBC, serum biochemical tests etc). 21 patients out of 30 (70 %) gave the history of exposure to smoking passively during childhood or later life time. Out of these 21 patients, 3 of them had been exposed to smoking during childhood and adolescence, 7 patients during adulthood, 11 patients during both childhood and later lifetime. It's a well-known finding that exposure to cigarette smoking, dusts, fumes and other kinds of air pollution could

cause the development of childhood -respiratory tract infections and COPD (5) and our results support these findings too.

The most important factor for the development of COPD is a!-antitrypsin deficiency which is a genetic defect (6). We measured serum cii-antitrypsin levels low in 4 (13,3%) patients. It has been stated that there is a [-antitrypsin deficiency in less than 1 % of COPD patients in the U.S. However, we selected our study group from nonsmoker people and they haven't been exposed to occupational hazards for the development of COPD, so the higher ratio of selecting patients with low serum level of a!-antitrypsin is not an unexpected finding in our study. These findings should be verified by genetic studies and those patients found to be carrying low serum AAT levels should be regarded as index cases so that family research studies should be further carried out. What we have done is to find out patients with low serum levels of AAT to show its countribution to environmental factors. We aimed to find out how much the environmental effects and personal characteristics infract in the development of COPD. So we didn't perform the Pi-typing genetically for those patients. The treshold protective level of serum AAT is 80 mg / dl or 11 um, is 35% of normal levels (7,8). But, in PiMZ heterozygous people with serum AAT levels of 57% of normal and PiSS persons with 52% of normal serum level of AAT, this much deficiency of serum AAT is informed to be one of the risk increasing factors, rather than a definitive one, for the development of emphysema (6). Those 4 patients with low serum AAT levels in our study had the values between 127-138 mg /dl. Also four other patients had serum AAT levels at the lower limit of normal range which is 140 mg/dl. So we have concluded that AAT deficiency has contributed to other risk factors for the development of COPD. It is well known that AAT deficiency can cause the onset of cirrhosis in adults and in 10 % of infants with PiZZ genotype hepatic dysfunction may occur during neonatal period and also cirrhosis may settle down in a low percentage of these infants with AAT deficiency (9). Any of these situations hasn't been found in our patients.

Low birthweight and frequent airway infections during childhood are also other risk factors of COPD. The incidence of developing COPD in adulthood has ben found to be higher in patients who undergone pulmonary infections in first two years of life when compared to people who didn't. But this incidence has been said not to be higher in females with COPD (9). We couldn't get enough data on this situation. However, we have got some history of pulmonary infections in the past of five patients but we couldn't get any pathologic finding in their chest X-ray films and tomographic examinations of their thorax. That's why we have considered that the respiratory infections in their early childhood have had no influence on the development of COPD in those patients.

It is known that family tendency has a role on the development of COPD. In family studies, it has been shown that first degree relatives of patients with COPD represent higher incidence of having airway obsruction and chronic bronchitis with respect to control group (10). 15 (50 %) of our patients gave the family history of COPD. This fact is supporting the genetic predominance of COPD.

In occupational studies, it has been shown that there is an increase in the prevalence of chronic airway obstruction in persons who work at places polluted by chemical dusts and fumes (11). One (3,3%o) of our patients gave the history of exposure to coal -dusts for 5 years (she performed coal - delivery twenty years ago). We haven't found any other occupational hazard for the development of COPD in other patients; 22 (73,3%) patients are housewife, one (3,3%) is ex-teacher (retired of work), two *(6,6%)* patients are ex-civilservants (retired) one (3,3%>) patient is ex-nurse (midwife, retired of work), one (3,3) is a farmer, two (6,6%) patients are ex- cleaning workers (servants at school, retired).

Air pollution is a definitive risk factor which causes development of COPD and its acute crisis. In studies made on air pollution it has been shown that it increases the mortality risk of COPD patients on days having higher amounts of rough particle densities (12).

The number of patients who have been living in urban for life long is 8 (26,6%), who have been living in rural is 10 (33,3%)) and who have been to both areas is 12 (40%). Those living in urban have been staying in Ankara where air pollution has

been a common problem .The patients living in rural haven't been exposed to industrial air pollutants but, 5 out of 10 living in rural for life long have been subject to indoor airpollution by means of biologic fuels and fumes of firewood burnt. We have seen that those 12 (40%) patients of both urban and rural places have been affected by biologic fumes and indoor- air pollutants. The mean duration of exposure is 38,30 years.

As Doosing et al. reported the study made on 40 nonsmoker COPD patients, 23 patients out of 40 gave the history of exposure to fumes of biologic fuels and firewood burnt where as there was a similar history in 5 % of healthy control group. So it's a risk factor to get exposed to smokes of biologic fuels and firewood burnt for females in S.Arabia. and also they made pathologic examinations after fiberoptic bronchoscopy performed onto 10 nonsmoker female patients living in rural who have been eposed to same kind of fumes and indoor air pollutants, so they reported results as such that there were intracellular anthracotic deposits, metaplastic changes and also distortion in mucous secretion and local defense factors. It has been shown by these findings that indoor air pollution plays an important role in the etiology of chronic bronchitis (13,14).

By using these findings we can conclude that COPD developes and gets worse in the presence of AAT deficiency in females who are exposed to indoor air pollution by means of passive smoking, fumes of biologic fuels and firewood burnt since their childhood, especially if they're living in rural even if they haven't been exposed to industrial air pollution. If these patients are smoking cigarette, the clinical picture gets worse in terms of prognosis. As a result, in patients with COPD, active and passive smoking, out- and in-door air pollution which are examples of preventable risk factors play an important role in the pathogenesis of disease in addition to genetic predisposition and AAT deficiency. It is considered to decrease prevalence, mortality and morbidity of COPD by eliminating preventable factors. It's important to inform this point to the patients of COPD and other people in the population.

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