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Epidemiological features of Turkish patients with sarcoidosis

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Summary
Epidemiological characteristics of sarcoidosis differ according to geographical distribution. The aim of our study was to disclose epidemiological characteristics in our country.

The data was collected from investigators, who sent information on newly-diagnosed patients via internet.

In 2 years 198 female and 95 male patients were enrolled to the study (f/m:2.08). Mean age of patients was 44 ± 13 years (17–90). Mean age of male patients was 38 ± 12 while mean age of female patients was 48 ± 13 ($p < 0.001$). 73.4% of patients were nonsmokers (85.4% of females; 48.4% of males; ($p < 0.001$)). About 50% of our 293 patients were housewives. Familial sarcoidosis was found in 3 patients' first degree relatives. Estimated annual incidence of sarcoidosis for Turkey was calculated as 4 per 100,000 person.

According to our study, 2/3 of sarcoidosis patients were women; mean age of patients was 45 and the disease began 10 years later in female patients. 80% of patients were nonsmokers; negative relation between sarcoidosis and smoking was evident especially in women. Familial sarcoidosis frequency was lower compared to other studies in the literature. There was no occupational exposure history in our patients. Our incidence rate, is similar with the results of other European studies.

Introduction

Sarcoidosis is a systemic granulomatous disease of unknown etiology, that affects primarily the lungs. There are evidences about the etiological role of genetic factors,[1–9] infectious agents,[1,10–16] environmental agents [1,17–20] and occupational exposures,[1,17,21,22] but the cause(s) of sarcoidosis still remain unknown. Data about the incidence of the disease are variable. Annual incidence of sarcoidosis is reported to be between 0.1 and 81 per 100,000; estimates of prevalence range from 0.1 to 640 per 100,000.

Sarcoidosis is known as a disease of young adults.[23,24] In Scandinavian and Japanese studies, a second peak incidence is reported in women over 50 years old. Most studies showed higher incidence in women.[23–28] However, other many studies do not confirm this finding.[1,17,29,30] Sarcoidosis shows different ethnic and geographic distribution. In, studies from U.S.A., the prevalence of sarcoidosis in blacks is higher than in whites. It becomes more prevalent in the areas far from equator. In Europe, it is reported more frequently in northern countries.

There is an inverse relationship between the risk of sarcoidosis and the likelihood of being a smoker. Smoking rate was found between 20 and 55% in sarcoidosis patients.[31–33]

Familial cases have been reported since 1920s.[2,6,8,34,35] Results of studies for the frequency of familial sarcoidosis are different; frequency rates of familial cases range from 1 to 19%. It is reported 3–3.5 times more frequently in African–American patients.[8,23]

Akkaynak reported the first patient with pulmonary sarcoidosis in Turkey in 1953.[36] There have been case series after this first report. Gurkan et al. reviewed these studies.[37] Demirkok et al. reported data of 275 patients from a single institution between 1966 and 2004.[38] None of these studies has the power to represent the real profile of Turkish patients. So further research is needed to display the real status of sarcoidosis in our country.

Material and methods

This study was organized and conducted by Turkish Thoracic Society Clinical Problems Study Group.

Turkish Thoracic Society (TTS), is the largest national, scientific and educational respiratory society in our country. It has over 2400 members, most of which are chest physicians. This study was announced via internet to all members of the TTS. Twenty five investigators from 19 centers of 12 cities in 6 different regions attended to the study. These investigators are employed in general outpatient clinics of pulmonology departments. These twelve cities are shown in yellow in Fig. 1.

Study protocol and case record forms were sent to investigators via internet. Newly diagnosed cases were recorded to electronic case record forms; these forms were collected by one of the study investigators.

Cases newly diagnosed as sarcoidosis between 1st June 2004 and 31st May 2006 were enrolled to the study. Existing cases were ruled out. According to the study protocol, cases with compatible clinical and radiological findings and histological non-caseating granulomas were accepted as sarcoidosis, after exclusion of other causes of granulomas such as tuberculosis, Crohn's disease etc. Histological confirmation was not a necessity for patients with classical Löfgren's syndrome.

Statistical analysis was done by SPSS 13 package programme. Groups were compared using chi-square and student's t test; p values <0.05 were considered as statistically significant.

Estimated annual incidence was calculated with the following method: The total number of patients who applied annually to the outpatient clinics of all the institutions in the study-cities was determined (A). The number of patients who applied to the outpatient clinics of the study-centers was calculated (B). The ratio of A/B was established (C). This ratio was used to calculate the estimated number of sarcoidosis patients (D) with the help of the reported number of sarcoidosis patients (E) ($D = EC$).

Figure 1 Cities where the study investigators worked.

According to the population of these 12 cities (F), annual incidence (G) of the disease was estimated ($G = D/F$).

Results

In 2 years 198 female and 95 male patients were enrolled to the study (F/M:2.08). Mean age was 44 ± 13 (min:17, max:90). Mean age of male patients was 38 ± 12 while mean age of female patients was 48 ± 13 ($p < 0.001$) (Figs. 2 and 3).

Eight (2.7%) of the patients were 70 years old or elder; 7 (87.5%) of them were females. Twenty three (7.8%) of the cases were persons over 65 years of age and 19 (83%) of them were women.

Familial sarcoidosis was found in 3 patients' first degree relatives. There was no sarcoidosis history in second degree relatives of patients.

73.4% of patients were nonsmokers, 20.8% current smokers (11 ± 7 pack.years); 5.8% ex-smokers (average quitting time was 7 ± 7 years ago). 85.4% of females but 48.4% of males were nonsmokers ($p < 0.001$). Cumulative cigarette consumption was 11 ± 9 pack.years for men and 11 ± 10 pack.years for women ($p > 0.05$). Occupations of patients are shown in Table 1.

The total number of annual applications to outpatient clinics of centers participated in the study was 189,000. 293 cases were reported from these centers in 2 years. Therefore, annually 146.5 of 189,000 applications per year were patients with sarcoidosis. The sum of annual application to all state and university hospitals of cities attended to the study was 1,400,000. Estimated number of patients with sarcoidosis was 1084. Total population of cities attended to the study was 27,000,000. Estimated annual incidence of sarcoidosis for Turkey was calculated as 4 per 100,000 person.

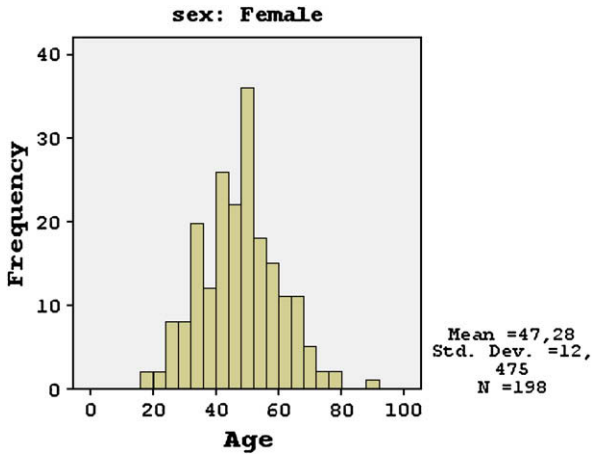

Figure 2 Age distribution of female patients.

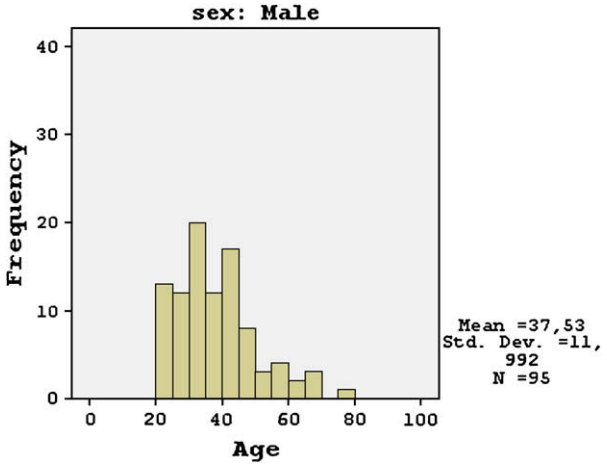

Figure 3 Age distribution of male patients.

Table 1 Occupations of patients.

Occupation	*n*	%
Housewife	147	50.2
Office worker, teacher, student	47	16.0
Health care worker (physician, nurse, etc.)	11	3.8
Agricultural worker	9	3.1
Textile worker	8	2.7
Tobacco worker	3	1.0
Electric technician	3	1.0
Driver	3	1.0
Chemistry sector worker	2	0.7
Worker producing glass	2	0.7
Building contractor	2	0.7
Barber	2	0.7
Unoccupied	2	0.7
Firefighter	1	0.3
Miner	1	0.3
Cook	1	0.3
Ceramic worker	1	0.3
Shoemaker	1	0.3
Worker	16	5.5
Other	31	10.6

Discussion

To our knowledge, this is the first incidence study about sarcoidosis in Turkey; the incidence was found 4 per 100,000. Epidemiological studies from other countries showed different incidence rates. This may be explained by geographic and ethnic variations. In addition, diagnostic difficulties, and different methods of the studies may cause different incidence results. Mainly four different methods are used for calculating incidence rates; 1) mass radiological screening programs, 2) evaluation of countries' database, 3) questionnaire studies and 4) autopsy studies. Every method has its own deficiencies. Chest X-ray screening programs were done on selected populations. Second method includes cases with definite diagnosis. However, it is thought that the real incidence rate should be higher than that of calculated as cases with definite diagnosis, because 31–68% of patients diagnosed with chest X-ray screening were asymptomatic.[25,27,39–41] The case number of the autopsy studies are 10 times greater than the numbers of other methods.

In the United Kingdom, incidence rate was found 8.2 per 100,000 in a radiological screening trial of persons vaccinated with BCG aged 15–25 in 1965.[27] In 1973, incidence rate for sarcoidosis in the U.S. navy was found 5.8 per 100,000 for white men and 60.1 per 100,000 for black men.[42] In another study the same method was applied between 1975 and 2001 in the U.S. navy, incidence rate was 3.5 per 100,000 for Whites, and 24.9 per 100,000 for Blacks.[43] In the U.S.A., between 1967 and 1987, incidence rate was 4.8 per 100,000 according to the national database.[44] Incidence rate was found 7.2 per 100,000 using the national database in Denmark.[45] In Finland incidence was found 11.4 per 100,000, with mass chest X-ray screening.[46] In questionnaire studies including items for specific diagnostic criteria, incidence rate was 0.17 per 100,000 in Belgium and 0.03 per 100,000 in Korea.[47,48] In the U.K. the review of patients' database between 1991 and 2003 revealed the incidence as 5 per 100,000.[49]

Our result is quite similar with the results of the last British incidence study.

Mean age of overall patients is 43 years. The mean age of females is 10 years more than mean age of males. Sarcoidosis has a tendency to be diagnosed about age 50 in females according to our results. In ATS/ERS/WASOG 1999 Statement on Sarcoidosis it was reported that, the disease showed a predilection under the age 40, peaking in those aged between 20 and 29; but in Scandinavian countries in Japan there was a second peak of incidence in women over age 50.[24] In the ACCESS study the peak age group was 35–45, and the male patients were younger than the female patients.[50] In the recent U.K. study most of the patients were between 35 and 55 years of age.[49] Byg et al. found the mean age in males and females as 38 and 45 respectively. These results are similar to ours.[45]

2.7% of our patients were aged 70 years or elder. Except one, all of these patients were female. Standyk et al. found that 7.8% of patients were individuals over 65 years of age.[51] In our study this ratio was also 7.8%, too. 83% of these patients were females. Chevalet et al. showed that 70% of patients over age 70 were women.[52] These findings suggest that sarcoidosis is diagnosed in older ages in females than those in males.

Hillerdal et al. and Byg et al. showed that the disease has two peak incidence points in 30 and 50 years of age[25,45]; which we could not confirm.

We diagnosed the disease two times more often in women. Most studies in the literature reported increased risk in women in comparison to men. In the ACCESS study female/male ratio was 1.77, but in the British study this ratio was 1.11.[49,50] Investigators suggested that these different results were related to geographical variations.

Approximately 75% of our patients were nonsmokers. The smoking history shows some difference in female and male patients. 15% of female patients but 50% of male patients were smokers. In normal population 65% of males and 25% of females smoke in Turkey. Smokers were less frequent in both female and male patients with sarcoidosis than those in normal population according to our results. However negative correlation between sarcoidosis and smoking was striking especially in women. Smoking patients' ratio was lower in other studies of the literature.[18,31–33] Negative correlation between sarcoidosis and smoking was also supported in the ACCESS study.[53]

Frequency of familial sarcoidosis was found 1% in our study. McGrath et al. found this ratio as 5.91% in patients in the U.K.[54] In the study published in 2001 by ACCESS research group, familial sarcoidosis was found in 3% of patients.[35] There are very different results about frequency of familial sarcoidosis in the literature. In our study familial sarcoidosis is less frequent than those in other studies from different countries.

About 50% of our 293 patients were housewives. 16% of patients were office worker, teacher or students. The majority of the patients had not any occupational

exposure. Previous studies reported increased frequency of sarcoidosis in firefighters,[55,56] health care workers,[29,33,57] soldiers,[58,59] wood workers[60,61]; but in the ACCESS study, a clear relation between sarcoidosis and occupation could not be disclosed.[53] Our finding, that 50% of patients were housewives, is compatible with this information.

Our incidence rate is in parallel with the results of other European studies. As nearly half of the patients are asymptomatic, the real number of cases and the incidence rate probably should be higher.[42] In addition not all the institutions in the country attended to the study, so our results may not show the exact number of patients. As there is no standardized data recording system for all diseases in our country at present; we do not have a more reliable method to calculate the incidence of sarcoidosis. Many centers from all geographical regions of Turkey attended to our study. Approximately 1/7 of the population of cities included in the study were sampled. Therefore this study most probably is able to represent the current status of sarcoidosis in Turkey.

According to our study, 2/3 of sarcoidosis patients were women; mean age of patients was 45 and the disease began 10 years later in female patients. 80% of patients were nonsmokers; negative relation between sarcoidosis and smoking was evident especially in women. Familial sarcoidosis frequency was lower than other studies in the literature. There was no occupational exposure history in our patients.

Conflict of interest statement

Neither author has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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