

## Examining the frequency of occupational exposures and environmental hazards in patients with sarcoidosis

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### ABSTRACT

**Introduction and objectives:** Sarcoidosis was recognized more than 120 years ago and remains a confusing disease to diagnose, with the cause hard to be identified. Exposure to numerous occupational and environmental factors is one of the risk factors of the disease. The aim of this study was to investigate the frequency of occupational exposures and environmental hazards in patients with sarcoidosis.

**Methods** This is a cross-sectional and descriptive study conducted on all sarcoidosis patients referred to a respiratory referral hospital in Tehran (Iran) in 2020. To collect data a standard questionnaire was used through interviews with patients that included occupational exposures and environmental hazards at work and at home.

**Results** The results of the present study showed that the average age of sarcoidosis patients participating in the study was 48.8±9.8 years. Eighty percent of patients with sarcoidosis were chronic and the rest were acute. The results of this study showed that 12% of the patients had "high humidity" in the work environment before the definite diagnosis and the onset of sarcoidosis. 11% of the patients had "water damage to appliances, ceilings, tiles or carpets" in the environment. 10% of patients reported "unpleasant and stale odors" in the workplace before the definitive diagnosis and onset of sarcoidosis, and 5% of patients reported "contact with animals in the workplace". Regarding the consumption of smoke and nicotine, 10% of patients with sarcoidosis were smokers and 3% used hookah.

**Conclusion:** As stated in the literature, work and environmental factors can be effective in sarcoidosis. However, determining the exact role of each of these factors and their effectiveness in causing the disease requires further research.

**Keywords:** Sarcoidosis, occupational exposure, environmental conditions

### Introduction

Sarcoidosis was recognized more than 120 years ago and remains a confusing disease to diagnose, with the cause hard to be identified (1). The highest rate of this disease has been reported in Northern European and African-American people, especially in women, and less in Japan (2, 3). The difference in its incidence and prevalence is related to age, gender, ethnic origin and geographical location. Sarcoidosis is rare in young people under 15 years old and old people over 70 years old. Exposure to the smell of mold, insecticides or metal processing industries is one of the risk factors (4, 5). Sarcoidosis is usually sporadic but familial in 3-9% of cases (6). Most

studies have shown that genetic predisposition and environmental factors contribute to the development of the disease. In terms of immunity, it can be said that sarcoidosis is a severe immune response to an antigen that has not been known so far. There is no evidence that it is an infectious disease and there is no definitive treatment for it. The only treatment is to change the course of granulomatosis and its clinical consequences. For more than 20 years, some researchers have hypothesized that in order to develop sarcoidosis, a person must not only be exposed to an antigen that can be delivered to TCD4+ lymphocytes by antigen-presenting cells, but that this must also occur in an inflammatory environment. Antigen in the lung, skin and other organs leads to the proliferation

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of T cells, differentiation and release of inflammatory cytokines, and attracts other cells to that environment and thus leads to the promotion of granuloma formation in the presence of two things: antigens and auxiliary signals aimed at an innate immune response. Case reports and small case collections over the years have suggested that a variety of mineral dusts (such as silicates, man-made mineral fibers), microbes, protein antigens, alkaline dusts, and alkalis can play the role of this "second blow"[\(7\)](#). In fact, the implication of many studies is that the risk of sarcoidosis is increased among people who are exposed to very high levels of these irritants. The history of exposure to such work environments should be carefully noted and collected to identify the potential of the workplace to cause sarcoidosis.

There are various evidences that show that certain workplaces are associated with the risk of sarcoidosis. The strength of this association has varied across studies, however a number of lines of evidence have emerged from these studies. First, as shown by the National Institutes of Health Studies, a case-control etiology study for sarcoidosis implicates germ-rich work environments in association with the disease. These locations include water sources that serve as reservoirs for microbial contamination and are used as sprays, agricultural sites rich in protein and mold antigens, and water-damaged work environments exposed to plant rust/mildew. Second, a number of studies consider employment in metal industries to be involved in the disease. Not surprisingly, it is well established that a number of metals can lead to granulomatous inflammation, such as beryllium, zirconium, rare earth elements, and aluminum. Thirdly, work environments that produce a high level of mineral particles are considered as a place with a higher risk for the development of sarcoidosis. Examples include exposure to wood greenhouses, talc, synthetic fibers, hard rock dust (silica), intensive agricultural activities, and other related occupations[\(8\)](#). Finally, an increased risk of sarcoidosis has been reported among those who have certain occupations, such as workers in the logging industry[\(9\)](#), firefighters[\(10, 11\)](#), marines[\(12, 13\)](#), workers in the wood, stone, and[\(14, 15\)](#) wool industries. Environmental factors play a significant role in the pathology of sarcoidosis and induce the clinical phenotype of sarcoidosis and thus have consequences for the patient's life. There is less information about environmental factors, especially those that are effective in the development of sarcoidosis, especially factors that promote the chronic and acute phenotype of sarcoidosis, which in some cases lead to premature death. The aim of this study was to investigate the frequency of occupational exposures and environmental hazards in patients with sarcoidosis.

## Procedure

The current research was a cross-sectional and descriptive study. The population included all people with sarcoidosis who visited the sarcoidosis clinic of a respiratory referral hospital in Tehran (Iran) from the beginning of 2020 to the end of 2020. In this study, 100 patients were included in the study by census method. There were two sources of information from which the study data were collected: Primary sources: Questionnaire forms completed by patients with definite diagnosis of sarcoidosis at Masih Deneshvari Center. Secondary sources: Information related to the course of the disease, response to treatment, complications or mortality during the follow-up of the patients was recorded in the patients' files by the project colleagues at the clinic. Inclusion criteria include: Having sarcoidosis, being literate, completing the ethical consent form. Exclusion criteria include: Patients who do not want to participate in the study, patients who withdraw from the study before the monthly follow-up, people who have active tuberculosis or who have been receiving anti-tuberculosis treatment were excluded from this plan. To investigate occupational exposures and environmental hazards with sarcoidosis, the plan was first approved by the ethical committee of the sarcoidosis research center of Masih Daneshvari Hospital. At the beginning of the project, written informed consent was obtained from the participants. Then questionnaires were provided to the participants. The standard questionnaire was completed through an interview with each of the patients in this project, the questions of which include: two-part questions, career history, hobbies, both at home and at work. The structure of the questionnaire included questions that examined the events of at least 6 working months of these people in detail. If the participant in this project was exposed to jobs that are considered to cause sarcoidosis and other respiratory tract diseases, the interviewer asked questions about occupational and environmental conditions for exactly 3 years before diagnosis and biopsy-confirmed granulomatosis. The questionnaires were completed based on the information in the patients' files. The obtained results were analyzed using SPSS software. In this study, descriptive analysis including mean, standard deviation, frequency and frequency percentage was used. Analysis was done using SPSS version 16 software.

## Results

The average age of sarcoidosis patients participating in the study was 48.8 years with a standard deviation of 9.8 years. The results of the table below show that 80% of patients with sarcoidosis were chronic and the rest were acute. Regarding the current employment status, 47% of sarcoidosis patients were employed and the rest were unemployed (Table-1).

**Table-1: Frequency distribution of disease severity and employment status in sarcoidosis patients**

Variable	Class	N	%
Type of sarcoidosis	Chronic	80	80.0
	Acute	20	20.0
Total		100	100.0
The current employment status	Employed	47	47.0
	Unemployed	53	53.0
Total		100	100.0

**Frequency distribution of occupational exposures and environmental hazards based on work list**

The results showed that only 1% of the patients before the time of definitive diagnosis and the onset of sarcoidosis were cotton factory worker, "information processing technician, typist, programmer", mill worker, "machine operator technician, assembler or supervisor", technician They were electricians, exposed to radioactive materials at work, flower sellers, quarry workers, preschool or kindergarten teachers.

The results showed that only 2% of the patients, before the definitive diagnosis and the onset of sarcoidosis, were building painters, home nurses, dentists or dental construction workers, textile workers, plastic production

workers, salesmen, masonry or polishing workers, middle school teachers and the high school and kitchen workers food and food preparation. Also, 3% of the patients were working in cosmetics, building demolition workers, advertising, print, drivers, pottery workers and welders before the time of definitive diagnosis and the onset of sarcoidosis. Finally, 5% of patients were farmers and ranchers before the definitive diagnosis and the onset of sarcoidosis.

None of the sarcoidosis patients are flight attendants, forest rangers, timber factory workers, glass factory workers, meat packing workers, meat transport workers, mine workers, postal workers, doctors, nurses, medical engineering technicians, resin workers, production workers, polyurethane foam, social worker or mental health worker, cotton spinning worker, sandblaster, foundry worker, 1st through 5th grade teacher, post-secondary teacher, tunnel construction worker, veterinarian, waitress, jewelry technician, dry cleaning worker, laborer, working in a rubber factory or in a pet store. The frequency distribution of other occupational exposures and environmental hazards in the office or in the work environment is presented in Table 2.

**Table2. Frequency distribution of some occupational exposures and environmental hazards in the office or at work**

Variable	Class	N	%
High humidity in the work environment	Never	88	88.0
	before the mentioned period (before the definitive diagnosis period and the onset of the disease)	12	12.0
	Employed or terminated after the period	0	0.0
Water damage to appliances, ceilings, tiles or carpets in the workplace	Never	89	89.0
	before the mentioned period (before the definitive diagnosis period and the onset of the disease)	11	11.0
	Employed or terminated after the period	0	0.0
Visible dirt outside the toilet in the workplace	Never	97	97.0
	before the mentioned period (before the definitive diagnosis period and the onset of the disease)	3	3.0
	Employed or terminated after the period	0	0.0
Unpleasant smells in the workplace	Never	89	89.0
	before the mentioned period (before the definitive diagnosis period and the onset of the disease)	10	10.0
	Employed or terminated after the period	1	1.0
Exposure to animals in the workplace	No	95	95.0
	Yes	5	5.0
Total		100	100.0

**Frequency distribution of environmental hazards based on residence**

The results of the table below show that only 1% of patients were exposed to aluminum, chromium, cobalt, gold, nickel, platinum, titanium and zirconium before the definitive diagnosis and the onset of sarcoidosis. Also,

only 2% of patients were exposed to insecticides or pesticides and exposed to hair spray before the definitive diagnosis and onset of sarcoidosis. 3% of patients were exposed to talc, beryllium, and silica before the definitive diagnosis and onset of sarcoidosis. 3% of patients were exposed to talc, beryllium, and silica before the definitive diagnosis and onset of sarcoidosis. The results showed

that 5% of patients reported being exposed to dust caused by plants such as flax before the definitive diagnosis and the onset of sarcoidosis. The frequency distribution of other environmental hazards in the place of residence is presented in Table 3.

Regarding the consumption of smoke and nicotine, the results of this study showed that 10% of patients with sarcoidosis were smokers and 3% used hookah. Also, 5% and 3% of patients reported smoking by another person at "home" and "at work", respectively.

**Table3. Frequency distribution of the status of some environmental hazards in the place of residence**

Variable	Class	N	%
Using a wood or charcoal stove to heat the house	Yes	88	88.0
	No	12	12.0
Mold in the interior of the bathroom	Never	88	88.0
	Finished before the period	11	11.0
	Existing or terminated after the period	1	1.0
Water leakage in the house	Never	89	89.0
	Finished before the period	9	9.0
	Existing or terminated after the period	2	2.0
Mice in the house	Never	84	84.0
	Finished before the period	11	11.0
	Existing or terminated after the period	5	5.0
Large insects in the house	Never	82	82.0
	Finished before the period	13	13.0
	Existing or terminated after the period	5	5.0
A dog in the house	Never	87	87.0
	Finished before the period	11	11.0
	Existing or terminated after the period	2	2.0
Pigeons in the house	Never	92	92.0
	Finished before the period	8	8.0
	Existing or terminated after the period	0	0.0
Total		100	100.0

## Discussion

Sarcoidosis is a multiorgan, granulomatous disease of unknown etiology. There is increasing evidence that sarcoidosis can be observed in the workplace, where there is exposure to foreign antigens and inorganic agents of inflammation, and these factors increase the immune response of granulomatous magnolia. It is also possible that sarcoidosis has more than one cause(7). Several environmental risk factors associated with sarcoidosis prevalence have previously been identified in epidemiological studies, including major exposure to water damage, work in the metal industry, motorcycle manufacturing, wood burning, and machining. The highest exposure to sarcoidosis in a number of studies was associated with air transport, hairdressing, wood dust, population density, being a dental technician, working in the medical and health sector, and furniture design(4).

The results of the present study showed that the average age of sarcoidosis patients participating in the study was 48.8 years. In the study of Morimoto et al., this disease was observed in all age groups from 0 to 86 years old, but it was reported very rarely in people less than 20 or more than 80 years old (16). In the study by Deubelbeiss et al., the average age of patients hospitalized for sarcoidosis in Switzerland was 55 years, and the average age at initial diagnosis was 45 years(4). Eighty percent of patients with sarcoidosis were chronic and the rest were acute.

Based on occupational exposures and environmental hazards based on the work list, only 1% of patients before

the time of definite diagnosis and the onset of sarcoidosis are cotton factory worker, information processing technician, typist, programmer, mill worker, machine operator technician, assembler or supervisor", electrician technician, occupational exposure to radioactive materials, florist, quarry worker, preschool or kindergarten teacher. Only 2% of the patients, before the definitive diagnosis and the onset of sarcoidosis, were building painters, home nurses, dentists or dental construction workers, textile workers, plastic production workers, salesmen, masonry or polishing workers, middle school teachers and the high school and kitchen workers food and food preparation. Finally, 5% of patients were farmers and ranchers before the definitive diagnosis and the onset of sarcoidosis. The data of the study by Deubelbeiss et al. showed a relationship between veterinary activities and the regional prevalence of sarcoidosis, while there was a relationship between the activities of dental assistants, social work activities, and activities related to the hospital and human health and the regional prevalence of sarcoidosis (4).

The results of this study showed that 12% of the patients had "high humidity" in the workplace before the definitive diagnosis and the onset of sarcoidosis. And 11% of patients also stated the situation of "water damage to equipment, ceiling, tiles or carpets" in the workplace. 3% of patients reported "obvious dirt outside the toilet" in the workplace before the definitive diagnosis and onset of sarcoidosis, and 10% of patients reported "unpleasant and

old odors" in the workplace. 5% of patients stated "exposure to animals in the workplace" before the definitive diagnosis and onset of sarcoidosis. In the Deubelbeiss study in Switzerland, it was reported that the prevalence of sarcoidosis is not the same in different regions and there is a relationship between the regional prevalence of sarcoidosis and the water supply industry, as well as between service activities such as washing textiles, collecting, purifying and distributing water and the regional prevalence of sarcoidosis. Statistically significant correlation was reported. (4).

Frequency distribution of the of environmental hazards based on residence, show that only 1% of patients were exposed to aluminum, chromium, cobalt, gold, nickel, platinum, titanium and zirconium before the definitive diagnosis and the onset of sarcoidosis. Also, only 2% of patients were exposed to insecticides or pesticides and exposed to hair spray before the definitive diagnosis and onset of sarcoidosis. 3% of patients were exposed to talc, beryllium, and silica before the definitive diagnosis and onset of sarcoidosis. The results also showed that 5% of patients reported exposure to dust caused by plants such as flax before the definitive diagnosis and onset of sarcoidosis. 11% of patients stated the presence of mold in the interior of the bathroom and the presence of mice in the house before the definitive diagnosis and the onset of sarcoidosis. 13% of patients reported the presence of large insects at home before the definitive diagnosis and onset of sarcoidosis, and 11% of patients reported the presence of dogs at home. In this study, none of the sarcoidosis patients reported the presence of frogs or salamanders at home.

In the study of Ramos-Casals et al., a higher risk of sarcoidosis was reported in people using central air conditioning or using coal/wood stoves, fireplaces, humidifiers, and private water sources; While the use of household insecticides does not increase the risk(17). Also in the study of Ramos-Casals et al., exposure to other household factors was negatively associated with sarcoidosis, including household pillow/pillow stuffing, exposure to children (including home care for other people or other children), and pets (cats, fish tanks and animal dust) (17). Also, Ramos-Casals et al. state that the main epidemiological studies have reported some leisure activities as protective factors, including having fish tanks or pet cats, bird watching/handling, exposure to indoor/hot pools(17).

Also, for a long time, nanoparticles have been predicted as a potential trigger of sarcoidosis based on their size and composition. Several recent toxicological studies have increased the importance of considering nanoparticles as a class of particles that may contribute to granuloma formation(7). Previously, Song et al. reported in a research that investigations conducted on injured workers in a spray paint center showed the presence of silica

nanoparticles in the lungs of patients and these nanoparticles may be partially responsible for the disease reported in these workers(18). In the study of Morimoto et al., abnormal absorption of gallium was diagnosed in 87.6% of 565 patients with sarcoidosis by surgical method (16). In the Deubelbeiss study, it was reported that there is a relationship between the regional frequency of sarcoidosis and the important areas of the metal industry and machinery production(4). Also, the data from the study by Deubelbeiss et al supports the hypothesis that areas with higher burden in the specific metal processing industry have a higher frequency of sarcoidosis. Whether these observations are related to the use of beryllium is not yet known, as allergic reactions to other metals may also play a role(4).

Regarding the consumption of smoke and nicotine, the results of this study showed that 10% of patients with sarcoidosis were smokers and 3% used hookah. Also, 5% and 3% of patients reported smoking by another person at "home" and "at work", respectively. Exposure to passive smoking was negatively associated with sarcoidosis in the study by Ramos-Casals et al (17). Ramos-Casals et al. state that in most case-control studies from the Netherlands, France, England, and the United States, an inverse relationship between smoking and the incidence of sarcoidosis has been reported (17).

One of the strengths of the present study was the measurement of various occupational and environmental exposures and a relatively high sample size, as well as the spread of patients from different parts of Iran. However, this study was also associated with limitations, such as the absence of a comparison group for analytical analysis.

## Conclusion

As stated in previous studies, occupational and environmental factors can be effective in sarcoidosis. However, determining the exact role of each of these factors and their effectiveness in causing the disease requires more research. It is suggested that studies with other research methods, including studies with a control group with a large sample size, investigate the exact effect of environmental and occupational factors on causing the disease.

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## Competing interests

The authors declare that they have no competing interests.

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