Occupational Medicine, 2025, **75**, 58–64
https://doi.org/10.1093/occmed/kqae137
Advance access publication 13 January 2025

OXFORD

Occupational exposure and sarcoidosis: a case-control study in three countries

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Background: Preceding studies of environmental and occupational risk factors of sarcoidosis yielded inconsistent findings.
Aims: We aimed to ascertain the occupational risk factors for sarcoidosis in a case-control study.

Methods: A total of 237 sarcoidosis patients with a histologically confirmed diagnosis were matched with 474 controls for sex and age (median 49, interquartile range 37; 60 years) recruited from the university hospitals and outpatient centres in Belarus, Kazakhstan and the Russian Federation. Ever and cumulative (considering years and hours per week) exposure to 24 occupational factors were analysed using logistic regression.

Results: In the overall sample of 711 subjects, 50% were females and any occupational exposure was more prevalent in cases compared to controls (60% versus 40%, $P < 0.001$). Current daily smoking as opposed to ex-smoking was associated with the lower risk of the outcome. Adjusted for smoking, age, sex and a few other exposures, ever-exposure to hay in agriculture (odds ratio (OR) 3.64 (95% confidence interval (CI) 1.26; 10.50)), engine exhausts (OR 2.94 (95% CI 1.14; 7.54)) and printing equipment (OR 1.66 (95% 1.03; 2.68)) was associated with sarcoidosis. The effect was also positive for cumulative exposure to hay in agriculture (OR 2.02 (95% CI 1.00; 4.07)), stone dust (OR 1.07 (95% CI 1.01; 1.14)) and engine exhausts (OR 1.18 (95% CI 1.03; 1.38)) and was stronger in never-smokers and subjects 40 years and older.

Conclusions: Widespread occupational exposures may increase the risk of sarcoidosis, but further research is needed to elucidate the complex interplay of environmental and occupational factors in the epidemiology of sarcoidosis.

INTRODUCTION

Exposure to vapours, gases, dust and fumes in the workplace commonly contributes to the development of chronic respiratory diseases. The burden of certain respiratory conditions varies significantly in occupational settings, as indicated by a recent comprehensive review encompassing the majority of non-malignant respiratory ailments [1]. In sarcoidosis, a chronic inflammatory granulomatous disease frequently involving the respiratory tract, occupational exposures ranged from 0% to 54%, with a weighted meta-proportion of 30% (95% CI 17–45%) according to pooled estimates [1]. The studies included in this review were primarily comprised of case series or case-control investigations

Key learning points

What is already known about this subject:

- Selected occupational exposures were inconsistently associated with sarcoidosis across studies, but recent studies elucidated the contribution of crystalline silica.

What are the new findings:

- Exposure to hay in agriculture, stone dust, engine exhausts and even printing equipment is associated with a significantly greater odds of sarcoidosis, and the effect may be stronger in subjects over 40 and never-smokers.

How might this impact on policy or clinical practice in the foreseeable future:

- Knowing occupational risk factors for sarcoidosis may guide prevention strategies for the disease.

with limited sample sizes. A need for more robust studies for the identification of causal factors, facilitating appropriate patient management through the removal of affected individuals from environments contributing to the disease, has been noted [2].

The aetiology of sarcoidosis is uncertain, but likely causative agents have been identified [2]. Research, seeking to identify causative agents has included potential occupational exposures. However, statistical associations were either not identified [3] or were weakly established, including for sales professionals and labourers in veteran populations [4]. Notably, certain occupations such as firefighting and healthcare demonstrated associations, and intriguingly, protective effects of smoking in sarcoidosis were also detected in these investigations. Subsequent reports, including the ACCESS study with a substantial sample size (>700 cases), demonstrated positive associations between sarcoidosis and exposure to birds, teaching professions and the automobile industry [5]. Similarly, a study involving African-American siblings revealed positive associations with roles in education, metal machining, metalworking, retail trade and transportation [6]. Furthermore, an analysis of death certificates indicated associations with occupations in metalworking, healthcare, education, sales, banking and administration [7].

More recently, the impact of silica and metal exposure has been investigated. A noteworthy case-control study, the largest of its kind, establisheded a robust correlation between silica exposure and sarcoidosis [8]. However, despite its extensive sample size, this study did not investigate other potential exposures. Aligning with a mounting body of evidence linking sarcoidosis to silica dust, another recent report underscored that pulmonary sarcoidosis, as distinct from involvement in other organs, was more prevalent among individuals exposed to inorganic dust [9]. Notably, the methodologies employed by older and more recent investigations varied, leading to discrepancies in their findings, while also encompassing divergent study designs. Given the disparate exposure classifications, the occasional limitation of small sample sizes in certain studies and the persistent need for detailed verification of occupational history in sarcoidosis cases [10], the case-control study described here sought to explore occupations and occupational exposures associated with the risk of pulmonary sarcoidosis.

METHODS

This study received ethical approval from the Committee on Bioethics of the National Centre of Occupational Safety and Health (Belarus), al-Farabi Kazakh National University (Kazakhstan) and Sechenov First Moscow State Medical University (Russian Federation) and all participants provided informed consent before their involvement. The research employed a case-control design with a 1:2 matching ratio. Cases diagnosed with pulmonary sarcoidosis (identified as D86 using ICD10) in Belarus, the Russian Federation and Kazakhstan were selected from hospital records. Inclusion criteria encompassed prior hospitalization, a typical clinical presentation, histological confirmation of diagnosis and age above 18 years. All enrolled cases exhibited pulmonary sarcoidosis, some with concurrent extrapulmonary lesions. Hospitalizations for diagnostic verification, accompanied by laboratory and ancillary examinations, were a prerequisite for inclusion. Cases lacking histological confirmation were excluded during the sample formation stage.

Control subjects without sarcoidosis were randomly matched to cases based on age and sex within the same city. Control recruitment involved multiple sources, including subjects from a prior epidemiological study on the occupational burden of COPD [11]. Additional controls were obtained from outpatient facilities in Moscow and Minsk, provided they had no history of sarcoidosis-related hospitalization. For each case identified, we enrolled two age- and sex-matched controls in the same city where a case was included. Such controls did not have sarcoidosis, but could have other pulmonary, musculoskeletal, gastrointestinal and other diagnoses or their combinations. Inclusion criteria for controls were independent of their exposure status, contingent on consent and the matching process occurred after case verification and inclusion.

The sample size calculation employed a formula considering the odds ratio (OR) from prior studies, exposed controls proportion, Z-alpha for a two-tailed test and the case-control ratio to determine power. Assuming an anticipated effect size of OR 1.62 from the ACCESS study [5], Z-alpha of 1.96, and a 40% proportion of exposed controls, a 1:1 case-control ratio would necessitate 270 cases [12]. However, opting for a 1:2 ratio led to 202 cases and 404 controls, achieving 80% power. The study ultimately recruited 237 cases and 474 corresponding controls, yielding an 86% power with a 14% type II error.

Participants, both cases and controls, completed a comprehensive questionnaire in Russian following informed written consent. The survey gathered baseline demographic information, including birthdate, date of first diagnosis, sex, permanent residence, total years of work, highest education level attained, detailed smoking status (never, ex-, current daily, current occasional conventional cigarette smokers) and exercise frequency. Alcohol use was categorized as never, occasional small amounts, occasional moderate amounts and several times a week. A detailed occupational exposure history was captured through a

24-exposure questionnaire [13]. This tool allowed to verify ever-exposure, years of exposure, average duration of work week in hours and subsequently compute the cumulative exposure (Table 1, available as Supplementary data at *Occupational Medicine* online). The last question solicited participants to specify a major lifetime occupation.

Data were screened for normality using the Shapiro-Wilk test, with most continuous variables showing non-normal distribution. Consequently, non-parametric tests were employed for analysis. Binary variables were presented as frequencies or percentages, while continuous variables were summarized as medians with corresponding interquartile ranges (IQR). Mann-Whitney U-test and Kruskall-Wallis test were used for univariate comparisons of continuous variables.

The primary outcome of interest was the probability of being a case following one or a combination of exposures in the lifetime. To calculate such a probability, we first computed the distribution of exposures overall, and then in cases and controls, and elucidated significant differences between these groups in the exposure distribution using contingency tables and χ^2 tests. We also tested the distribution of smoking, classified either as never- or as ex- or current daily or occasional cigarette smoking; alcohol use as a categorical variable with four outcomes; highest attained education; marital status; regular exercise and the overall work duration or years in service. Occupational exposures found significantly associated with being a case in such univariate comparisons, including smoking status, we then consecutively tested in crude logistic regression models. For each occupational exposure, we had two variables, including a simple binary variable, named ever-exposure in the current analysis and a cumulative exposure as a continuous variable. Cumulative exposure was obtained from the total years of specific exposure multiplied by the average hours worked per week and divided by 40 (conventional week duration in hours). All regression models were run separately for ever- and cumulative exposure.

Variables found significantly associated with being a case we also checked for collinearity using variance inflation factor, but none was detected. Then they were included in the multivariate logistic regression models, where these exposures, age, sex and smoking were all adjusted for each other. We reported the ORs with the corresponding 95% confidence intervals (CI) for each predictor in all such models. Following general modelling for the entire sample and separately in men and women, we then narrowed the sample into those 40 years and older and reran all models in this group. A similar approach was used to test the associations in never-smokers. All statistical tests were completed in NCSS 2022 (Utah, USA), and the *P*-values of the tests were specified accordingly.

Table 1. Overall demographic portrait of the included cases and controls

	Overall	Cases	Controls
N (%)	711 (100)	237 (33)	474 (67)
Age, years (IQR)	49 (37; 60)	49 (37; 60)	49 (37; 60)
Females, *N* (%)	358 (50)	119 (50)	239 (50)
Smoking status, *N* (%)*			
Never	424 (60)	138 (58)	286 (60)
Former	150 (21)	68 (29)	82 (17)
Daily	126 (18)	26 (11)	100 (21)
Occasional	11 (1)	5 (2)	6 (2)
Highest attained education, *N* (%)			
Secondary school	8 (1)	3 (1)	5 (1)
High school	103 (14)	36 (15)	67 (14)
College	237 (33)	86 (36)	151 (32)
University	343 (49)	107 (46)	236 (50)
Academic degree	20 (3)	5 (2)	15 (3)
Marital status, *N* (%)			
Single	118 (17)	33 (14)	85 (18)
Married	523 (74)	183 (77)	340 (72)
Divorced	70 (9)	21 (9)	49 (10)
Overall years in service (IQR)	23 (12; 33)	23 (12; 35)	23 (12; 33)
Exercising 3 times a week, *N* (%)	205 (29)	69 (29)	136 (29)
Alcohol consumption, *N* (%)			
Never	259 (36)	74 (31)	185 (39)
Small amount sometimes	233 (33)	81 (34)	152 (32)
Moderate amounts sometimes	179 (25)	68 (29)	111 (23)
Few times a week	40 (6)	14 (6)	26 (6)
Any exposure, *N* (%)*	332 (47)	141 (60)	191 (40)

*$P < 0.05$.

RESULTS

The study's case-control ratio of 1:2 resulted in cases constituting one-third of the sample. Median age across participants was 49 years (IQR 37; 60), with no disparity between cases and controls due to age and sex matching. Gender distribution was even, with approximately half of the participants being female (Table 1). Smoking status demonstrated significant differences, with 18% of the overall sample being daily smokers and up to 60% being never-smokers. Notably, controls had a higher proportion of daily smokers compared to cases (21% versus 11%), while the trend was reversed for former smokers. This indicated that a substantial number of cases had quit smoking either prior to or around the time of diagnosis. Daily smokers in both cases and controls smoked a median of 10 cigarettes per day for 15 years. When comparing daily smoking intensity between cases and controls, no significant differences were observed in the number of smoked cigarettes (median 10 for both groups) or smoking duration (median 10 years for cases and 20 years for controls, $P > 0.05$).

Around one-third of the sample engaged in regular exercise (at least three times a week), and a majority were married. Nearly one-third reported never consuming alcohol. Univariate comparisons of marital status, education, work duration and alcohol consumption revealed no differences between cases and controls. Conversely, significant differences emerged in exposure patterns, with 60% of cases and 40% of controls having ever been exposed in the workplace. The most prevalent exposures included second-hand smoke in the workplace (29% of the sample), working with copying and printing equipment (18%) and exposure to car or engine exhaust (10%). Most other studied exposures were reported in <10% of cases. Univariate comparisons identified a significantly higher prevalence of ever-exposure for 50% of the studied exposures (12 out of 24) among cases (Table 2). Notably, 11 of these 12exposures were more prevalent in cases compared to controls; however, this pattern did not persist when considering cumulative exposure.

The first three exposures in the questionnaire related to metals. Grouping these exposures revealed a non-significant difference between cases and controls, with 23 cases (10%) and 34 controls (7%) exposed to metals. Among the 57 subjects exposed to metals, 77% mentioned iron/steel, 30% stainless steel, 26% copper, 32% aluminium, 19% brass, 23% bronze, 32% hard metals, 11% wolfram or cobalt, 11% zinc-coated plates, 16% dyed metal, 9% gold or silver, 9% tin, 9% lead and 7% cadmium. Multiple metals could be reported for a single worker.

Crude regression models indicated a positive association between ex-smoking and the outcome (crude OR 1.92, 95% CI 1.33; 2.78), while the association was opposite for current daily smoking (OR 0.46, 95% CI 0.29; 0.73), reflecting the observed smoking cessation pattern upon diagnosis. These crude models corroborated associations seen in Table 2 (Tables 2 and 3, available as Supplementary data at *Occupational Medicine* online). Adjusted models, accounting for exposures, smoking, age and sex, revealed that only three ever-exposures (exposure to hay in agriculture, car/diesel exhausts and printing equipment) were independently associated with sarcoidosis (Table 3). When expressed as cumulative years of exposure (Table 4), exposure to stone dust, hay in agriculture and car/diesel exhausts was associated with increased sarcoidosis risk.

Subgroup analysis of participants aged 40 and older (N = 485) reinforced these patterns, with generally stronger effects. In multivariate analysis, ever-exposure to hay in agriculture exhibited an OR of 4.64 (95% CI 1.50; 14.40), exposure to car or engine exhausts displayed an OR of 3.93 (95% CI 1.15; 13.44), and work with copying/printing equipment was associated with a doubled odds of sarcoidosis (OR 2.06, 95% CI 1.17; 3.65). Additionally, cumulative exposure to stone dust was linked to a 1.09-fold increased risk of sarcoidosis (95% CI 1.02; 1.16), while the OR for exposure to car or engine exhausts rose to 1.22

Table 2. Univariate comparisons of included exposures between cases and controls

	Cases		**Controls**	
	***N* (%) exposed**	**Cumulative exposure in years, median (IQR)**	***N* (%) exposed**	**Cumulative exposure in years, median (IQR)**
Sandblasting, grinding, milling or metal processing	10 (4)	6 (4.5; 19.3)	22 (5)	10 (2.8; 24)
Metal or steel production	6 (3)	24.5 (7.8; 39)	24 (5)	10.5 (4.3; 20)
Welding*	15 (6)	10 (5.24)	6 (1)	15 (12; 17.8)
Nickel or chrome plating	0 (0)	–	2 (0)	7.5 (3;12)
Stone dust (in a quarry, mine, with building demolition, in the foundry, with a furnace)*	19 (8)	14 (8; 25)	12 (2)	15 (10.5; 20)
Carbon or graphite powder*	1 (0)	15 (15;15)	12 (2)	13 (6.3; 25.3)
Glass wool*	13 (5)	5 (2; 8.5)	9 (2)	7 (5; 9)
Ceramics	4 (2)	6.5 (1.3; 14.8)	4 (1)	2 (1; 20.3)
Asbestos or asbestos-containing products	7 (3)	10 (2; 23)	8 (2)	12 (5.5; 24)
Poultry*	6 (3)	5 (2.8; 12)	2(0)	2 (1; 3)
Hay in agriculture*	19 (8)	10 (3; 18)	6 (1)	2 (0; 6)
Grain or flour	10 (4)	4.5 (1.8; 12.5)	9 (2)	9 (1; 24)
Timber or wood shavings*	11 (5)	1 (1; 3)	6 (1)	8.5 (1.8; 17.8)
Paper production	6 (3)	8 (3.3; 23.3)	5 (1)	15 (5.5; 25)
Natural or artificial fibres	7 (3)	15 (6; 27)	13 (3)	15 (1; 27)
Ionizing radiation	2 (1)	2.5 (2; 3)	2 (0)	7 (2; 12)
Solvents	17 (7)	7 (2; 13.5)	20 (4)	14 (3; 20)
Open fire	7 (3)	6 (5; 10)	6 (1)	5.5 (1.8; 27.8)
Car or engine exhausts (in a repair shop or garage)*	24 (10)	7.5 (2.3; 16.5)	11 (2)	10 (4; 20)
Irritating gases	14 (6)	9 (2.8; 16)	14 (3)	11.5 (4.5; 15.8)
Lubricating oils*	15 (6)	8 (2; 24)	8 (2)	9.5 (5.3; 27)
Isocyanate containing glue*	7 (3)	6 (1; 10)	3 (1)	16 (15; 26)
Second-hand smoke in the workplace*	68 (29)	13 (6; 25)	94 (20)	15 (8; 21)
Copying and printing equipment*	42 (18)	12 (4; 20)	50 (11)	11.5 (5; 18)

*P < 0.05 in the χ^2 test.

Table 3. The effect (as OR with the corresponding 95% CI) of selected ever-exposures included in the multivariate logistic regression overall and stratified by sex

Exposure	Overall (N = 711)	Men (N = 353)	Women (N = 358)
Welding	2.36 (0.67; 8.30)	2.61 (0.73; 9.40)	–
Stone dust (in a quarry, mine, with building demolition, in the foundry, with a furnace)	1.45 (0.60; 3.50)	0.72 (0.23; 2.28)	5.28 (0.99; 28.14)
Glass wool	2.15 (0.74; 6.28)	2.36 (0.74; 7.53)	5.16 (0.13; 197.7)
Poultry	3.26 (0.54; 19.56)	6.23 (0.33; 115.0)	2.36 (0.17; 33.15)
Hay in agriculture	3.64 (1.26; 10.50)	3.41 (0.84; 13.91)	5.64 (0.94; 33.99)
Timber or wood shavings	2.06 (0.59; 7.24)	1.84 (0.51; 6.68)	–
Car or engine exhausts (in a repair shop or garage)	2.94 (1.14; 7.54)	2.33 (0.76; 7.15)	Unstable
Lubricating oils	1.52 (0.48; 4.76)	2.50 (0.64; 9.69)	0.81 (0.07; 9.50)
Isocyanate containing glue	3.11 (0.55; 17.59)	4.59 (0.67; 31.52)	2.36 (0.67; 8.30)
Second-hand smoke in the workplace	1.26 (0.83; 1.91)	0.85 (0.48; 1.52)	Unstable
Copying and printing equipment	1.66 (1.03; 2.68)	1.67 (0.79; 3.52)	2.13 (1.11; 4.08)
Ex-smoking	1.61 (1.07; 2.45)	3.32 (1.88; 5.88)	0.67 (0.32; 1.39)
Daily smoking	0.41 (0.23; 0.72)	0.78 (0.41; 1.53)	0.11 (0.02; 0.49)

The model is adjusted for the variables shown, age and sex (except stratified by sex analyses).

Table 4. The effect (as OR with the corresponding 95% CI) of selected cumulative exposure included in the multivariate logistic regression overall and stratified by sex

Exposure	Overall (N = 711)	Men (N = 353)	Women (N = 358)
Stone dust (in a quarry, mine, with building demolition, in the foundry, with a furnace)	1.07 (1.01; 1.14)	1.02 (0.93; 1.13)	1.22 (0.90; 1.65)
Hay in agriculture	2.02 (1.00; 4.07)	1.50 (0.85; 2.67)	Unstable
Car or engine exhausts (in a repair shop or garage)	1.18 (1.03; 1.38)	1.09 (0.92; 1.29)	Unstable
Ex-smoking	1.80 (1.20; 2.69)	3.30 (1.92; 5.65)	0.82 (0.40; 1.64)
Daily smoking	0.47 (0.28; 0.80)	0.87 (0.48; 1.63)	0.14 (0.03; 0.58)

The model is adjusted for the variables shown, age and sex (except stratified by sex analyses).

(95% CI 1.04; 1.43). Notably, work with hay in agriculture exhibited no association with the outcome in this older subgroup.

When the analyses were stratified by sex, smoking remained significantly associated with sarcoidosis. However, most exposure variables were no more associated with the outcome, probably due to loss of power, most pronounced in women, given that fewer women were exposed (39% versus 55% in men). Further narrowing the analysis to never-smokers (N = 424) highlighted significant associations between ever-exposure to stone dust (OR 3.39, 95% CI 1.05; 10.09), hay in agriculture (OR 5.02, 95% CI 1.44; 17.46) and copying/printing equipment (OR 2.08, 95% CI 1.13; 3.86) in a model adjusted for exposures and each other (R^2 = 0.36). Adjusted for each other cumulative exposure model (R^2 = 0.21) demonstrated significant associations for stone dust (OR 1.10, 95% CI 1.01; 1.20) and hay in agriculture (OR 17.88, 95% CI 1.21; 264.61) with sarcoidosis.

DISCUSSION

The landscape of earlier publications on environmental and occupational risk factors for sarcoidosis varied significantly in terms of sample size, exposure classification and reported effects. In our sample of 711 subjects, maintaining a case:control ratio of 1:2 across three countries, we succeeded in confirming the previously established association between smoking and sarcoidosis. Exposure to stone dust, car or engine exhausts, hay in agriculture and work with copying/printing equipment demonstrated positive associations with sarcoidosis, independent of each other, where the latter are novel findings. These associations were particularly pronounced among subjects aged 40 years and older, with exposure to hay in agriculture exhibiting the strongest effect. It is of note that the pattern of significantly associated exposures remained consistent among never-smokers.

Historically, the contribution of occupation and occupational hazards to sarcoidosis has received minimal attention in Soviet literature. Our recent systematic review of Russian literature from former Soviet countries highlighted this gap, where only a few low-quality studies examined this aspect [14]. Exposure data for crystalline silica were not available for exposed cases or controls, but the positive association of exposure to stone dust with sarcoidosis in our cohort was consistent with earlier findings of the effect of silica. In a Swedish population register, the risk of the disease was 27% greater in those exposed with even greater effect in younger men [8]. This study was the largest ever to report the effect, but it was, however, limited to only one exposure. Such findings were consistent with another study from Sweden where cases were recruited from the construction industry [15]. In 371 cases, they demonstrated some 83% increase in the risk of the disease in medium to highly exposed workers. In addition, 12 cases were reported from a cohort of 506 hard-rock miners with known respirable crystalline silica levels in the air [16], in which authors conclude on the likely association of employment with the diagnosis. Furthermore, high immunoreactivity to silica was found in the greater number of sarcoidosis patients compared to controls in another study [17].

No association of exposure to silica with sarcoidosis was found in the ACCESS [5] and a recent report from Israel [18], possibly due to unreliable silica exposure estimates. The use of a more detailed 24-item questionnaire in our study was an attempt to reduce such exposure misclassification. Similarly, the effect of metals could not be robustly confirmed across studies demonstrating some positive association expressed either as higher immunoreactivity [17] or as ever working in metal machining of metalworking [6] or even greater mortality rates in sarcoidosis patients exposed to metals [7], or no association in the multivariate analyses [5]. Our study also failed to confirm such an association.

An earlier observation of the positive association of work in agriculture with sarcoidosis was also found in this study. An almost 1.5-fold greater risk of sarcoidosis in the agricultural workers in the ACCESS study [5] is consistent with a 2-fold greater risk of the outcome in those exposed to hay in agriculture in our report. Work in farming and agriculture was also the most prevalent exposure in a small group of sarcoidosis cases [19]. Birds may be another occupational and environmental exposure with an ambiguous effect. The positive association of exposure to birds in [5] could not be confirmed in our cohort. Furthermore, the observation of stronger effect of most significant predictors in the older group in our study was also reported in the preceding publications. We hypothesize this could be associated with more accumulated years of exposure in the older worker groups.

Cigarette smoking is one of the most important risk factors studied in sarcoidosis patients from the very first published studies [3]. Many publications concluded that smoking had a protective effects for the onset of sarcoidosis, and the effects spanned from ever-smoking [5] to current daily smoking. Smoking induces a range of inflammatory responses and has been shown to cause most respiratory diseases or worsen their prognosis, and sarcoidosis could be one of them [20,21]. In the occupational groups, smoking is even more important and shows a complex interplay with a healthy worker effect [22–26]. Significantly lower daily smoking in our cases compared to the general population in all three included countries [11,27,28] further reaffirms the notation that many with sarcoidosis cases quit smoking.

The major limitation of our study was the use of only questionnaire data for exposure classification, given that objective exposure assessment data were not available. In our study, as in most preceding case-control studies, which almost always rely on the retrospective exposure data, such exposure misclassification was likely. We also believe that some differential misclassification of exposure was present [29]. However, our approach to mitigate such recall bias was to select controls, not from the healthy group, but from the general population with other diseases [30], such as cancer, cardiovascular conditions, etc. Additionally, while we matched subjects by sex and age, other confounders like socioeconomic status [31–33] or BMI were not accounted for. We also understand that some unmeasured confounding was present. Additionally, the questionnaire did not consider exposures of interest outside those at work. Finally, our study lacked testing for beryllium sensitivity, which is recommended for sarcoidosis patients.

In conclusion, our study fills an evidence gap by exploring the occupational contribution to sarcoidosis, an aspect historically understudied in the included countries. We have now demonstrated that exposure to stone dust, hay in agriculture, engine exhausts and even copying/printing equipment display positive associations with sarcoidosis. While our findings provide valuable insights into potential risk factors, further research is required to better understand the complex interplay of occupational exposures, smoking and other variables in sarcoidosis development.

ACKNOWLEDGEMENTS

We thank all participants for their consent to participate. We also thank Marina Dehara for her contribution to data analysis.

FUNDING

There was no funding for this study.

COMPETING INTERESTS

None declared.

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