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Is living close to ophiolites related to asbestos related diseases? Cross-sectional study

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Summary
Objective: To determine the rate of pleural plaques and malignant mesothelioma and other factors that affect people living close to ophiolites.
Methods: The study population was comprised of 2970 volunteers who resided <10 km from an ophiolitic unit. Control group comprised of 157 residents >25 km from ophiolites. Information gathered from the patients included presence of pleural plaques on chest X-ray, distance from ophiolites, gender, smoking status, duration of asbestos exposure, and body mass index (BMI). Mineralogical analysis of soil and rock samples was performed by X-ray diffraction.
Results: Among the 2970 study participants, those who lived close to ophiolites, 9.8% had asbestos related disease (3 malignant mesothelioma, 289 pleural plaques). No asbestos related disease (ARD) was identified in the control group. Male gender (OR: 2.63, 95% 1.9—3.5, $p < 0.001$), advanced age (5% increase for every year $p < 0.001$), residential proximity to ophiolites (for every 1 km proximity, a 12% increase $p < 0.001$), and low BMI (for every 1 unit decrease, 3.6% increase $p < 0.001$) were associated with increased risk of ARD.
Conclusion: The rate of ARD is higher in residents living close to ophiolites. Important risk factors for developing ARD were age, male gender, proximity to an ophiolite site, and low BMI.

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Introduction

Environmental asbestos exposure has been reported in the countries of Turkey,[1] Greece,[2] Italy,[3] the USA,[4] and New Caledonia.[5] Ophiolites, which are sections of the earth's oceanic crust and the underlying upper mantle that were uplifted and exposed above sea level onto continental crustal rocks by geologic processes, are known sources of naturally occurring asbestos (NOA).[6] In rural part of Turkey, residents living close to ophiolites use soil from ophiolitic area in their homes, because of its insulation properties and water tightness. Close relationship was detected between distance to ophiolites and birthplace of the patients with mesothelioma and pleural plaques in a registration based, case control study.[7] Based on these results, we planned a cross-sectional study in the same geographical area in order to investigate the relation between living close to ophiolites, as well as other possible factors and asbestos-related diseases (ARD).

Material and methods

Subject selection

Forty-eight of 68 villages of Yildizeli district and Sivas center within a 10 km range to ophiolite units were randomly selected. Simple randomization was performed to determine subjects by sampling 15% of each village. For the control group, subjects were from 6 villages $>$25 km to ophiolites. Inclusion criteria were; to be $\geq$35 years and lived $>$20 years in that village. A database search of the Sivas health directorate confirmed that within the last 10 years no patient from the control villages had an ARD.

To determine the location of villages with respect to ophiolites, we used a geological map of Sivas province made by the General Directorate of Mineral Research and Exploration of Turkey.[8] Fig. 1 shows the villages included in the study. Distribution of ophiolites has been made more obvious by subtracting other geological units from the original map. For any village outside an ophiolitic area, the beeline distance between the center of the settlement and the edge of the nearest ophiolite area was calculated using the Google Earth software program.

A total of 3127 subjects were evaluated. From these, 16 subjects were excluded from the study for the following reasons: costodiaphragmatic sinus bluntness (5), reticulonodular opacities (4), tuberculosis sequel plus pleural calcification (1), pleural effusion (3 bilateral with cardiomegaly, and one chronic effusion of unknown etiology), one suspect pleural thickness, and one round calcification. For the study group, 2970 volunteers (1140 male, 1830 female) came from 48 villages $<$10 km to ophiolites.

Informed consent was obtained from each participant. The study was approved by the Cumhuriyet University ethics committee.

Chest X-ray examination

The first interpretation of the chest X-rays was done on the examination day by a pulmonologist (MB) in order to decide on any further investigation of the patients. At the end of the study, final interpretations were carried out by 3 study investigators (MB, ID, and NDB) who were blinded to the residencies of the subjects. Discrete dense pleural opacities or linear structures, localized on the chest wall, diaphragm, pericardium, or mediastinum were considered to be caused by pleural plaques.

Mineralogical analysis

A total of 33 samples were randomly taken from indoor wall plasters as well as from sources of plasters from the villages close to or distant to ophiolite areas. Samples were analyzed by X-ray diffraction (XRD).

Statistical analysis

T-test, Mann–Whitney *U* test and, Chi-square tests were performed for statistical analysis. Logistic regression was used in the univariate and multivariate models to detect the dependent variables.

Results

Mean ages of study and control groups were 55.2 $\pm$ 13, 57.3 $\pm$ 16, respectively, with no gender or BMI difference between the groups (Table 1). No current or previous occupations or other possible causes for an exposure to asbestos were reported.[9] Almost all subjects were engaged in farming and livestock, only a few were officers, religious officials, and village headmen. Duration of residency in an adobe house was longer in the study group.

The clinical findings of subjects with and without ARD are summarized in Table 2. No ARD was identified in the control group, from villages close to ophiolites 290 patients with ARD were identified (3 with malignant mesothelioma, 287 with pleural plaques). ARD was more frequent in male subjects, in subjects living in an adobe house, and in subjects with a low BMI. The ARD rate increased with age. The lowest ARD rate was found in the 35–45 age range (6.0% male, 1.8% female). The prevalence was gradually increasing with age. The highest ARD rate was in the $\geq$75 group (28.6% male, 16.7% female).

Factors possibly affecting ARD risk in the study population were found as male gender, age, residential proximity to ophiolites, and decrease in BMI (Table 3).

Mineralogical analysis revealed fibrous minerals (primarily chrysotile) and lesser amounts of pectolite, brucite, hydrotalcite, and tremolite/actinolite in the villages close to ophiolites. No fibrous minerals were found in control villages.

Discussion

This is the first prospective study investigating the relation between distance to a geological structure-namely ophiolites and occurrence of ARD. It shows a 9.8% rate of ARD in participants from ophiolitic areas, which is associated with residential proximity to ophiolites, male gender, advanced age, and low BMI. It supports previous studies that report an

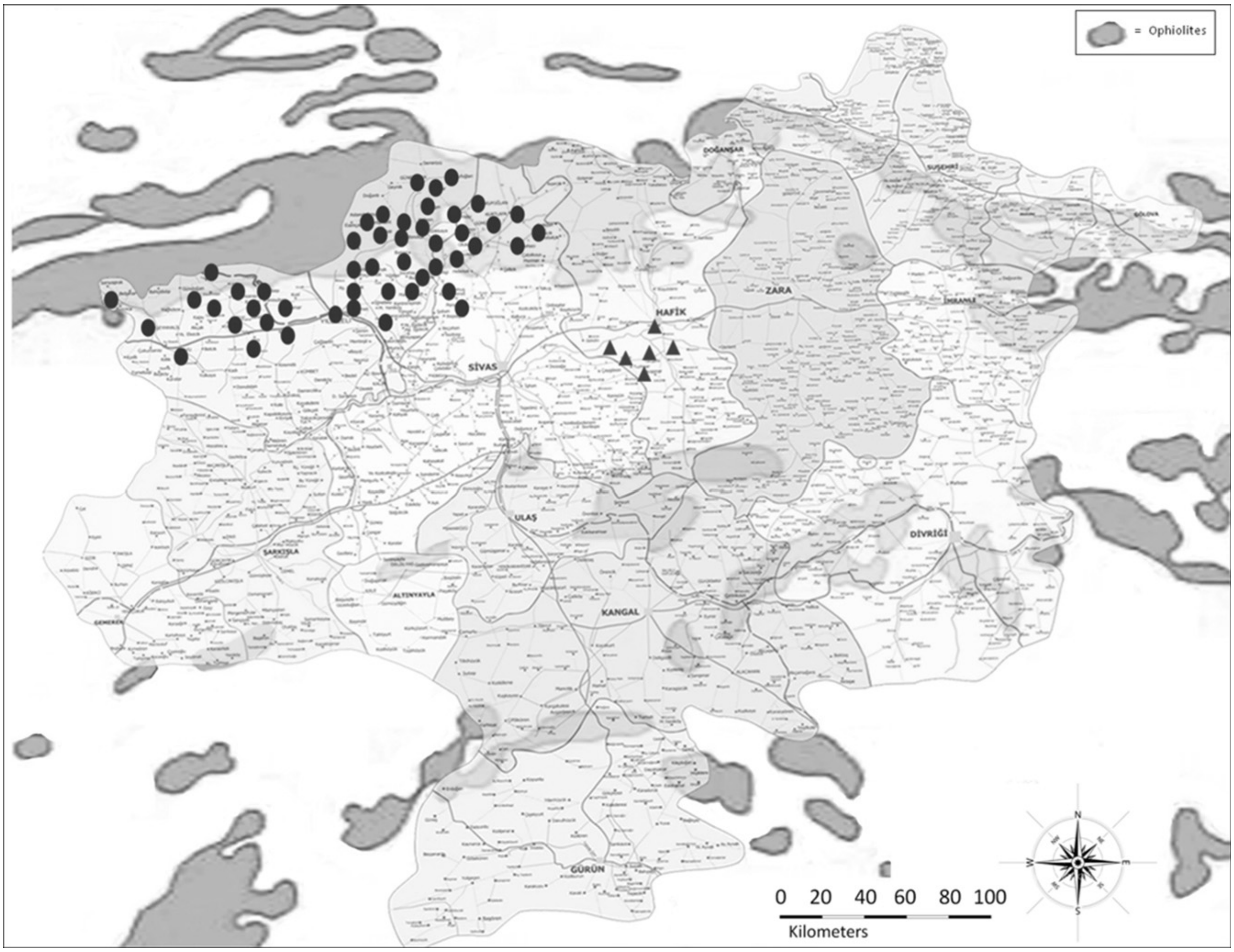

Figure 1 Map of Sivas province overlapped with modified geologic map. Patchy areas represent ophiolites; circles represents the villages close to ophiolities; and triangles represents the control villages located >25 km to nearest ophiolite.

elevated incidence of benign and malignant diseases caused by asbestos inhalation among people living in close vicinity to NOA sources and/or who had direct contact to asbestos via whitewash or plaster comprised of asbestos-containing soil.[1,2,10,11]

Data from the current study show an 8% decrease in risk of ARD for every 1 km of additional distance from ophiolites. A retrospective study from California revealed a 6.3% decrease in mesothelioma risk for every 10 km distance to NOA, but some of the mesothelioma patients had

Table 1 Demographic findings of study population.

		Subjects living within ≤10 km to ophiolites (n = 2970)	Subjects living >25 km to ophiolites (n = 157)
Male gender		38.4	41
Age		57.3 ± 14.6	55.2 ± 13.2
Living rate in adobe house		50.5	39.1
Median distance to ophiolites, km		0.873 (0–7.8)	26.1 (26.1–26.1)
Body mass index	Female	29.2 ± 5.7	29.0 ± 5.0
	Male	26.4 ± 4.4	26.1 ± 4.5
Asbestos related diseases	Total	9.8	0
	Male	17.1	0
	Female	5.2	0

Data are presented as mean ± SD or percentage or median (25th–75th percentile range).

Table 2 Demographic parameters of subjects with ARD and subjects with no ARD.

		Asbestos related diseases present 287 PP, 3 MM	No asbestos related diseases[a] 2680	p
Age		63.8 ± 11.7	54.2 ± 13	<0.001
Male gender		67.0	35.4	<0.001
Smoking	Never smoked	60.4	76.0	<0.001
	Former smoker	15.9	11.4	<0.001
	Smoker	23.6	12.6	<0.001
Body mass index	Male	25.5 ± 4.4	26.5 ± 4.3	0.002
	Female	28.2 ± 6.1	29.3 ± 5.6	0.07
Living rate in adobe house		61.6	49.4	<0.001
Median distance to ophiolites km		0 (0–9.57)	0.87 (0–9.04)	<0.001

Data are presented as mean ± SD or percentage or median (25th–75th percentile range). ARD = asbestos related diseases; MM = malignant mesothelioma; PP = pleural plaque.
[a] Subjects living at villages >25 km to ophiolites not included.

occupational exposure and it was conducted in a very large area (approximately 15-fold larger than Sivas province).[4] In a smaller surrounding, Kurumatani et al. found a similar relation between distance and sources of industrial asbestos.[12] A more recent report showed an increased risk of mesothelioma with proximity to serpentinite sources in New Caledonia.[5]

Yazıcıoglu discovered no gender difference in mesothelioma patients who had been exposed to tremolite asbestos,[13] nor did a study of pleural plaque patients from Metsovo, Greece.[14] On the other hand, Metintas et al. found that risk of pleural plaque due to environmental asbestos exposure was associated with male gender.[1] The great gender difference in the current study might be explained with the mobility of male subjects (e.g., farming on fields of ophiolite-containing soils). Males are exposed to both indoor and outdoor asbestos sources, whereas women are exposed primarily to indoor asbestos.

The response rate to our invitation was 76.8% in females and 47% in males. Still, the large number of subjects allowed us to investigate all parameters by adjusting for gender. Advanced age is associated with an increased risk of pleural plaque, reflecting longer duration of exposure. This finding supports previously published data.[1,15] Low BMI seems to be associated with ARD development in male subjects, yet no other study in the literature reported a relationship between BMI and ARD presence. Whether such a relationship is a reason for or a consequence of pleural plaque formation is unclear and should be assessed by further investigations.

X-ray diffraction analyses of soil and plaster samples confirmed the presence of serpentine minerals. Although samples were not assessed for asbestos minerals, tremolite fibers were detected in bronchoalveolar lavage fluid of patients with ARD from villages of Sivas in a previous study.[16]

Even though it is known that in other Anatolian provinces tremolite fibers were detected[1,11,13] this is the first field-based epidemiological study from the province Sivas.

The strengths of the current study are its cross-sectional design (with a control group), the absence of significant industrial sources of exposure to asbestos in the area, and the large number of subjects who participated.

A limitation of the study is the low sensitivity of chest X-rays, which can lead to under-diagnosis of small pleural plaques and/or pleural thickness. Pleural plaques might be more prevalent than our findings in this area. Ambient air sampling was not performed. Indoor and outdoor air sampling might help explain the great difference of pleural plaque rates between male and female subjects.

In conclusion, Sivas is one of several provinces in Anatolia with NOA, resulting in a high rate of pleural plaque in otherwise healthy subjects. It has been shown that males,

Table 3 Univariate and multivariate logistic regression of parameters for developing asbestos related diseases.

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Age, every 1 year increase	1.05 (1.04–1.07)	<0.001	1.05 (1.04–1.06)	<0.001
Male gender	3.67 (2.8–4.7)	<0.001	2.63 (1.9–3.5)	<0.001
Distance to ophiolites, every 1 km farther	0.92 (0.88–0.99)	<0.001	0.92 (0.88–0.96)	0.001
Living in adobe house	1.62 (1.27–2.08)	<0.001	1.27 (0.96–1.66)	0.083
Body mass index, every 1 unit increase	0.93 (0.90–0.95)	<0.001	0.96 (0.93–0.98)	0.006
Smoking[a]	2.33 (1.72–3.15)	<0.001	1.21 (0.89–1.65)	0.21

ARD = asbestos related diseases, CI = confidence interval.
[a] Subjects are considered "smoker" if they have smoked more than 1 pack-years even they are former smokers.

the elderly, and those residing close to ophiolites are at highest risk for occurrence of pleural plaques.

Conflict of interest statement

None declared.

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