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

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Asbestos;
Ophiolites;
Mesothelioma;
Pleural plaques

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, Greece, Italy, the USA, and New Caledonia. 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). 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. 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 ≥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. 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 cardiac involvement), 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 ± 13, 57.3 ± 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. 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 >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
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.\textsuperscript{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>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic findings of study population.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects living within ≤10 km to ophiolites (n = 2970)</td>
</tr>
<tr>
<td>Male gender</td>
<td>38.4</td>
</tr>
<tr>
<td>Age</td>
<td>57.3 ± 14.6</td>
</tr>
<tr>
<td>Living rate in adobe house</td>
<td>50.5</td>
</tr>
<tr>
<td>Median distance to ophiolites, km</td>
<td>0.873 (0–7.8)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>29.2 ± 5.7</td>
</tr>
<tr>
<td>Male</td>
<td>26.4 ± 4.4</td>
</tr>
<tr>
<td>Asbestos related diseases</td>
<td>Total</td>
</tr>
<tr>
<td>Male</td>
<td>17.1</td>
</tr>
<tr>
<td>Female</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or percentage or median (25th–75th percentile range).
Asbestos related diseases due to environmental exposure

Subjects living at villages

Subjects are considered “smoker” if they have smoked more than 1 pack-years even they are former smokers.

This finding supports previously published data.1,15 Low BMI of pleural plaque, reflecting longer duration of exposure.

Advanced age is associated with an increased risk allowed us to investigate all parameters by adjusting for

gender. 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.

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

<table>
<thead>
<tr>
<th>Asbestos related diseases present</th>
<th>No asbestos related diseases&lt;sup&gt;a&lt;/sup&gt;</th>
<th>&lt;sup&gt;p&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (287 PP, 3 MM)</td>
<td>63.8 ± 11.7</td>
<td>54.2 ± 13</td>
</tr>
<tr>
<td>Male gender</td>
<td>67.0</td>
<td>35.4</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>60.4</td>
<td>76.0</td>
</tr>
<tr>
<td>Former smoker</td>
<td>15.9</td>
<td>11.4</td>
</tr>
<tr>
<td>Smoker</td>
<td>23.6</td>
<td>12.6</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25.5 ± 4.4</td>
<td>26.5 ± 4.3</td>
</tr>
<tr>
<td>Female</td>
<td>28.2 ± 6.1</td>
<td>29.3 ± 5.6</td>
</tr>
<tr>
<td>Living rate in adobe house</td>
<td>61.6</td>
<td>49.4</td>
</tr>
<tr>
<td>Median distance to ophiolites km</td>
<td>0 (0–9.57)</td>
<td>0.87 (0–9.04)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or percentage or median (25th–75th percentile range). ARD = asbestos related diseases; MM = malignant mesothelioma; PP = pleural plaque.

<sup>a</sup> Subjects living at villages >25 km to ophiolites not included.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>&lt;sup&gt;p&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td>Age, every 1 year increase</td>
<td>1.05 (1.04–1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>3.67 (2.8–4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distance to ophiolites, every 1 km farther</td>
<td>0.92 (0.88–0.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Living in adobe house</td>
<td>1.62 (1.27–2.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, every 1 unit increase</td>
<td>0.93 (0.90–0.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.33 (1.72–3.15)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ARD = asbestos related diseases, CI = confidence interval.

<sup>a</sup> 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.

References