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REGULAR ARTICLE

High-risk mesothelioma relation to meteorological and geological condition and distance from naturally occurring asbestos

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Abstract
Objectives Very few studies have investigated the incidence and risk of malignant mesothelioma (MM) associated with distinct sources of asbestos exposure, especially exposure to naturally occurring asbestos (NOA).
Methods Subjects were MM, lung, and breast cancer patients who were diagnosed and followed in Diyarbakir Province between 2008 and 2013. The birthplaces of patients were displayed on a geologic map. Geological and meteorological effects on MM were analyzed by logistic regression.
Results A total of 180 MM, 368 breast, and 406 lung cancer patients were included. The median distance from birthplace to ophiolites was 6.26 km for MM, 31.06 km for lung, and 34.31 km for breast cancer ($p < 0.001$). The majority of MM cases were seen within 20 km from NOA areas. The MM incidence inside of NOA was 1059/100.000, and out of NOA was 397/100.000; this difference was significant ($p = 0.014$). The largest concentration of MM residential areas was within ±30° (34 residential areas 36.6 %) of the dominant wind direction. Most MM patients were found in or near the dominant wind direction, especially in the acute angle defined by the dominant wind direction. MM incidence was directly proportional to {[area of NOA (km^2)] * [cosine α of wind direction angle]} and was inversely proportional to the square of the distance ($R = 0.291$, $p = 0.023$).
Conclusions MM was higher near NOA and in the downwind direction. MM incidence and risk were affected by geological and meteorological factors.

Keywords Mesothelioma · Naturally occurring asbestos · Wind direction · Incidence · Risk

Introduction

Malignant mesothelioma (MM) is a tumor originating from the pleura, although the pericardium, peritoneum, or tunica vaginalis may be affected. The strong relationship between asbestos exposure and MM has been recognized since the early 1960s [1]. MM is generally caused by environmental and occupational asbestos exposure. Additionally, asbestos found in volcanic tuff has been shown to induce mesothelioma. MM resulting from environmental exposure to asbestos is a relatively common pleural cancer in some areas of Turkey [2].

In some developed countries, mesothelioma patients have been exposed to asbestos at work (occupational exposure). The term 'naturally occurring asbestos' (NOA) applies to minerals as natural components of soils or rocks, as opposed to the asbestos in commercial products, mining, or processing operations. Mining, road construction, agriculture, forestry, urban development, and natural weathering processes have all potentially contributed to release of asbestos fibers into the environment to some degree. If NOA is not disturbed and fibers are not released into the air, then it is not a health risk [3].

Due to domestic or neighborhood exposure to asbestos or other mineral fibers, an increased risk of mesothelioma

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has been found in several countries including Australia [4], South Africa [5], and Italy [6]. A relationship between environmental exposure to NOA and MM has been detected in Greece [7], New Caledonia [8], China [9], and Italy [10], but no research has studied the association between residential distance from environmental (non-occupational) asbestos and mesothelioma risk [11].

In Turkey, studies among residents of two Anatolian villages suggested that high incidence of MM results from environmental exposure to carcinogenic tremolite and erionite, a fibrous zeolite that is present in the volcanic tuff used as building stone [12]. MM is seen in southeastern Turkey due to environmental asbestos exposure [2, 13].

Many studies have investigated the effect of distance from NOA to the residential areas of MM patients [14, 15]. Only two studies have addressed the effect of meteorological conditions on MM [14, 16]. In those studies, the dominant wind direction influenced MM. However, a search of the literature for the field of NOA failed to find previous investigations addressing the combined effect of dominant wind direction and distance from NOA on MM incidence.

Ophiolitic rocks are highly dismembered and comprise undifferentiated mantle tectonites and gabbroic rocks. The highly serpentinized mantle tectonites are primarily composed of dunite and harzburgite. Serpentine, fibrous actinolite, amphibole, sericite, and kaolinite are secondary phases of these rocks [17].

This study aimed to investigate factors that affect MM incidence including geological, environmental, and meteorological conditions, dominant wind direction, distance to NOA, and rock type in an MM-prevalent region of Turkey. We aimed to investigate geological sites of ophiolites associated with different incidences of MM, lung, and breast cancer.

Materials and methods

In this retrospective study, a total of 180 pathologically verified MM, 368 breast and 406 lung cancer patients were included in the study who born in Diyarbakir Province were followed by the Dicle University Hospital in Diyarbakir-Turkey from January 2008 to December 2013.

Histological evaluation was performed on either surgical and/or necropsy material and patients with histologically proven MM, lung and breast cancer patients were included. Histochemical or immunohistochemical stains were used if necessary.

Data were obtained from medical record or interview to the patients. MM patients having occupational exposure history to asbestos were excluded. Domestic and para-occupational exposure to asbestos occurred among people living with asbestos workers or near asbestos-manufacturing plants were excluded. Environmental exposure in this study should come from naturally occurring asbestos only in study area. Non-occupational exposure in asbestos-insulated buildings was excluded. We also excluded another cancer history in this study.

Ethical approval was obtained from Dicle University Local Ethic Committee (Approval Number: 53).

The 180 MM patients were born and lived in 93 rural and urban locations in Diyarbakir Province. Patient birthplaces were determined from registry cards or were requested from the governmental registration office based on personal identity document numbers or other data such as birth date, parents' names, and so forth. MM patients whose birthplace could not be determined were excluded from the study.

The birthplaces of MM, lung, and breast cancer patients were located on a map of Diyarbakir Province, and settlement locations were determined with respect to ophiolite exposure as depicted on the geologic map of the General Directorate of Mineral Research and Exploration of Turkey [18]. In maps, we defined the sample location is the birthplaces of MM, lung, and breast cancer patients.

Figure 1 shows the distribution of ophiolites after exclusion of all other asbestos-free geologic units from the original map. Patient birthplaces were also identified as being within or outside NOA. In Diyarbakir, three NOA areas were identified (Fig. 1).

Annually dominant wind direction is from the northwest (Fig. 2). The predominant winds in the area blow at a mean annual speed of 1–2 m/s [19, 20].

Residential areas were defined settlement of birthplace patients. In this study, some of residential area was seen more than one patients. So we detected 180 MM patients in 93 residential areas.

The number of NOA areas, area sizes (km^2), and distances to residential areas from NOA (km) were calculated using the geologic map and an AutoCAD program. The distances to residential areas from NOA areas were determined from the geometric center of each NOA.

The location of the residential area relative to the angle of the dominant wind direction was calculated in radians from the nearest asbestos source in degrees (0°–360°) counterclockwise from North. The narrower the angle of wind direction is, the greater is its effect; therefore, the value of cosine α (cos α) was calculated for each angle α in radians (AR).

The incidence of MM was calculated as a residential area average population value between the years 2008 and 2013, and the number of MM cases who lived in this residential area during the same period was recorded. Incidence was calculated as the number of cases of mesothelioma per hundred thousand population (*n*/100,000).

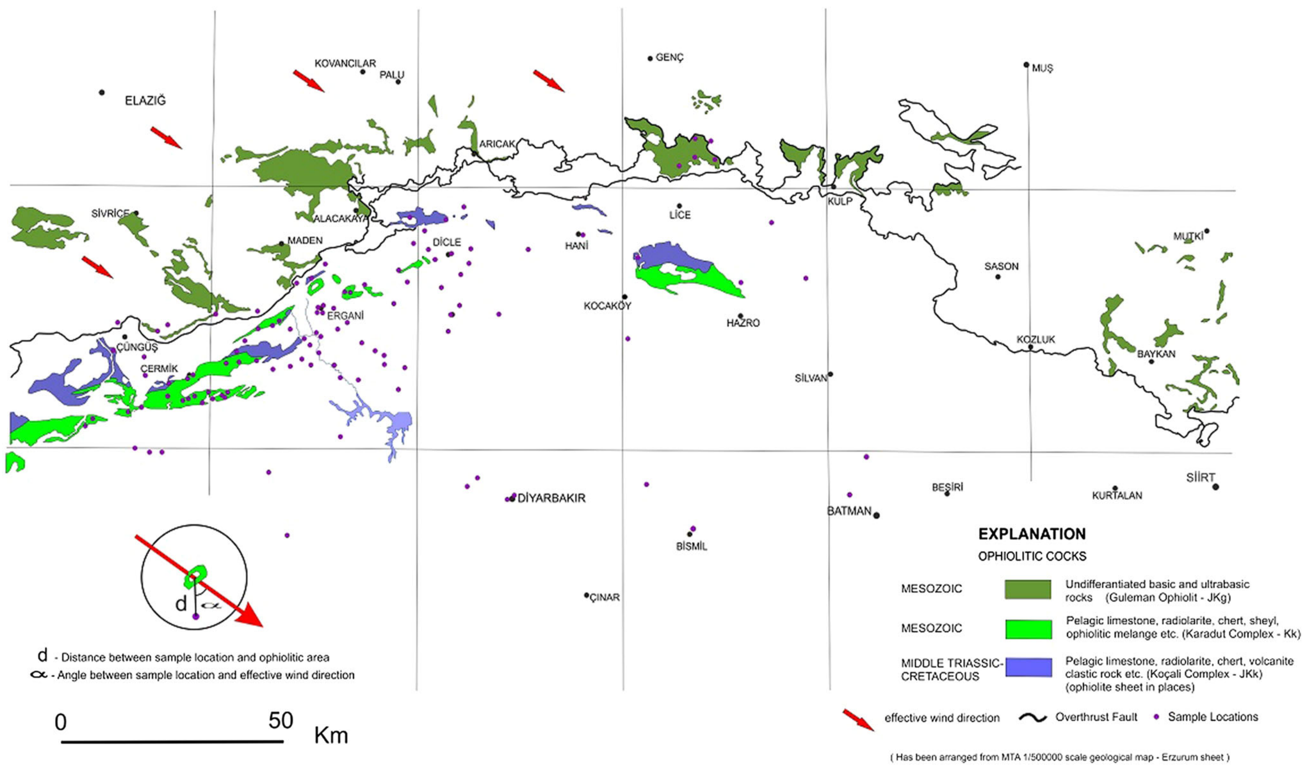

Fig. 1 Distribution of MM patients on geological map Diyarbakir Province

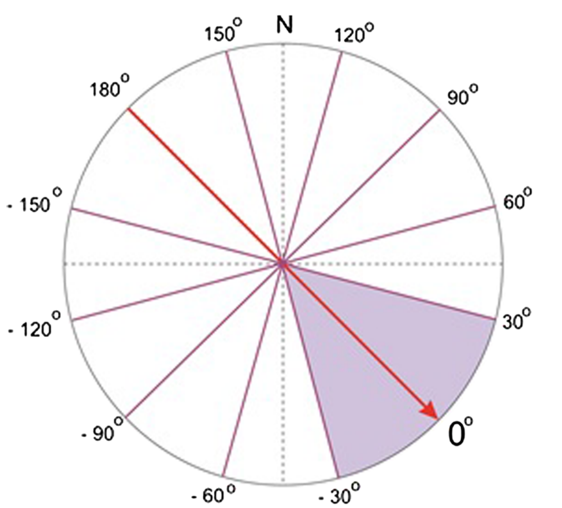

Fig. 2 Dominant win direction Diyarbakir Province and calculation of angle

Statistical analysis

Mean values and standard deviations were calculated for continuous variables. The normality of the variables was analyzed by the Kolmogorov–Smirnov test. Parametric tests were used to analyze normally distributed data.

The wind direction relative to the residential area was defined by 30° angles clockwise and counterclockwise and was classified into six categories (0°–30°, 30°–60°, 60°–90°, 90°–120°, 120°–150°, and 150°–180°) (Fig. 2).

Location determined by the number of mesothelioma residential areas was analyzed by Chi-square test relations between the angular regions. Residential areas were divided into two groups: those inside and those outside the NOA. Student's *t* test was used to compare mesothelioma incidence between the two groups.

Each residential area in or near the area of asbestos was divided into three groups by the rock properties of the area: Guleman ophiolite (JKg), the Koçali complex (JKk), and the Karadut complex (Kk) (Fig. 1); the incidence of these groups was determined by ANOVA testing.

Comparison with the two groups following ANOVA was done with post hoc Tukey test.

Curve-estimation regression models were used to determine the relationship between residential area distances from NOA (Fig. 1) and the cumulative number of MM patient cases at each distance. The model with the highest significant *R* value was considered the best model.

To determine the factors that predict MM incidence, a conditional backward linear regression analysis was used, with log (incidence) as the dependent variable and potential predictors (field area, distance, cos α, and rock type) as independent variables. Significance was taken as $p < 0.05$. Statistical analyses were performed using SPSS statistical program version 11.

Results

This study followed 180 MM patients from the university hospital from 2008 to 2013. The mean age of MM patients was 58.15 ± 12.21 (24–85) years; 104 (57.7 %) of the MM patients were male and 76 (42.3 %) were female.

Of the 368 breast cancer patients, 360 (98.4 %) were female and six (1.6 %) male. The mean age of the breast cancer patients was 48.8 years. Of the 406 lung cancer patients, 351 (86.5 %) were male and 55 (13.5 %) female. The mean age of the lung cancer patients was 59.9 years.

The number of environmental asbestos exposures according to patients' knowledge was 118. Most cases were within 5 km of an asbestos-containing area (Table 1).

The locations of MM patients' birthplaces are shown in Fig. 1. The locations of the breast cancer patient birthplaces are shown in Fig. 3a, and those of lung cancer patients in Fig. 3b.

Figures 1, 3 and Table 2 show that MM patients were much more likely to have been born within or close to an NOA than were patients with lung or breast cancer.

Thus, the median distance between birthplace and ophiolites was 6.26 km for MM patients, significantly closer to NOA areas than those of either breast or lung cancer ($p < 0.001$) patients (Table 2). Most MM patients were within 5 km of NOA areas, whereas the mean distance from NOA areas for lung and breast cancer patients were 34.31 and 31.06 km (Fig. 3a, b).

Seventeen NOA areas were identified in Diyarbakir (Fig. 1). The mean field area of these areas was 45.4 ± 45.4 km^2. The mean incidence of MM in 93 residential areas was 660.8/100,000 population. Of the 93 residential areas, 60 were <5 km from NOA areas.

We found the largest number of MM residential areas within ±30° of the dominant wind direction (34 residential areas, 36.6 %) (Fig. 3). The next greatest number of MM residential areas was in the 30°–60° sector centered on dominant wind direction (clockwise and counterclockwise), with 23 residential areas, or 24.7 %. The smallest number of MM residential areas was found in the direction opposite (±120°–150° and 150°–180°) the dominant wind direction (Fig. 3; Table 3).

Analysis of the incidence of MM in all residential areas revealed that this incidence was significantly higher in or near JKg and JKk rocks than it was in or near Kk (Table 4). The incidences of MM within asbestos source residential areas was 1059/100,000, and that outside source areas was 397/100,000; this difference was significant ($p = 0.014$).

When residential areas were divided into three categories (within NOA area, <10 km away, and >10 km away from NOA) (Table 5), the highest incidence of MM was found at the asbestos source, and the lowest incidence at >10 km distant from the source area; this incidence difference is also significant (Table 4).

To investigate the relationship between the cumulative numbers of cases and distance from NOA, curve estimation analysis were used by regression analysis, and the highest and most significant association was found in logarithmic models ($R^2 = 0.915$, $p < 0.001$) (Fig. 4).

As seen from the model, of 180 MM cases, the residences of the majority (150 cases) were within 20 km of NOA areas. Furthermore, MM incidence increased with increasing proximity to NOA and declined rapidly with increasing distance from the source.

The proportion of MM patients in residential areas outside of the NOA decreased in proportion to the distance from NOA and with increasing angles relative to the dominant wind direction. We used linear regression to predict the incidence of mesothelioma in any location using the field area of the NOA source, the cosine of the angle of the dominant wind direction, and distance from the asbestos source as the independent variables. The results of this linear regression showed that MM incidence changed in direct proportion to area (km^2) * cos α and was inversely proportional to the square of the distance from the source ($R = 0.291$, $p = 0.023$) (Table 6).

According to this model, the MM incidence increased with the size of the NOA area (km^2) multiplied by the cosine of the angle of the wind direction minus the square of the distance from the NOA.

Table 1 Characteristics of mesothelioma cases

Characteristics	Number of MM patients	%
Gender		
Male	**104**	**57.7**
Female	**76**	**42.3**
History of asbestos exposure		
Unknown	43	24.1
Negative	17	9.6
Positive	118	66.3
Cases distance of asbestos source (km)		
<5	131	73.6
5–25.5	37	20.8
>25.5	10	5.6

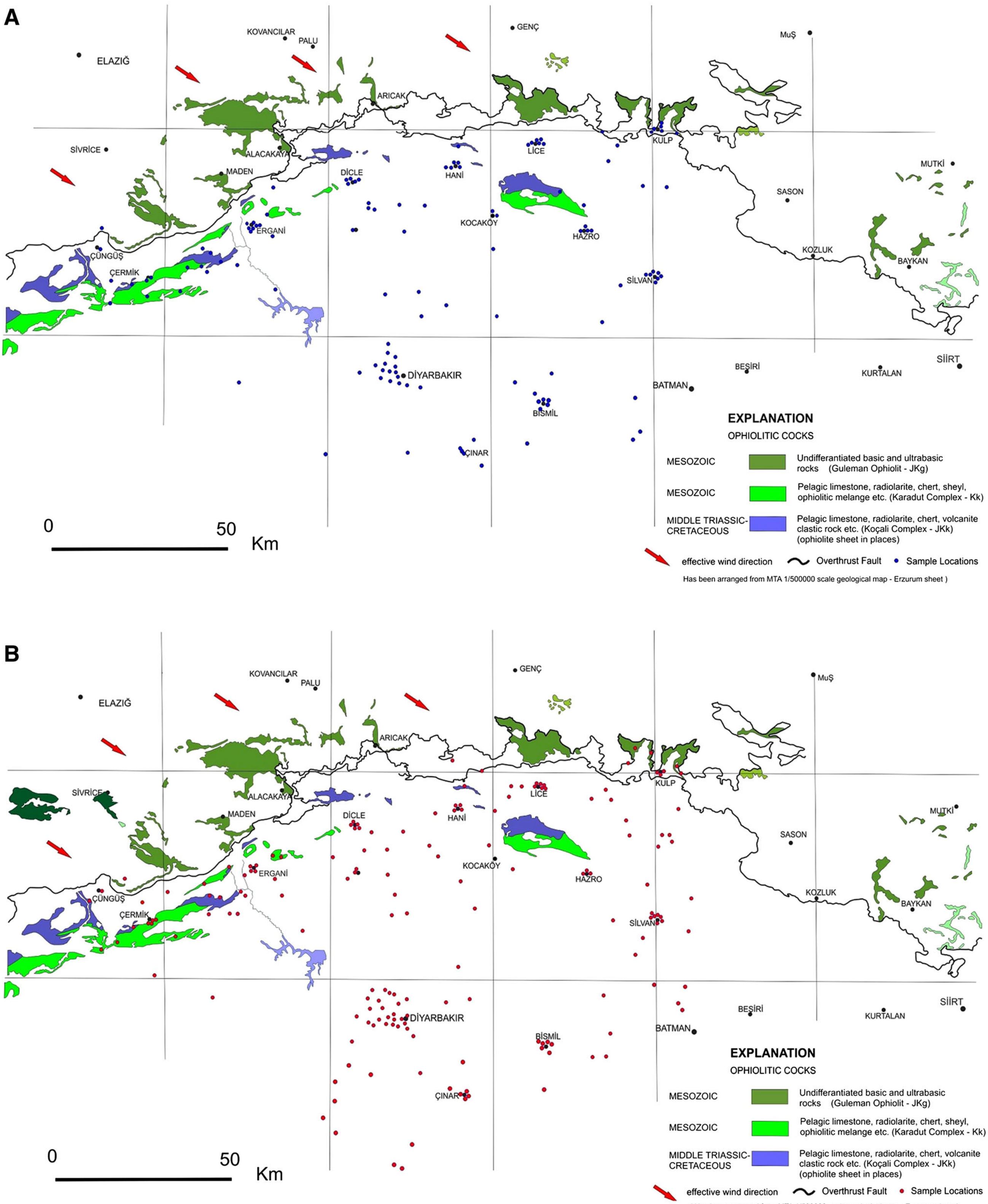

Fig. 3 **a** Distribution of breast cancer patients on geological map Diyarbakir Province. **b** Distribution of lung cancer patients on geological map Diyarbakir Province

Table 2 Comparison of distance between three case groups

Disease	*n*	Distance (km)	Standard deviation
Distance from source (km)			
Mesothelioma	180	6.26	11.52
Breast cancer	368	34.31	23.16
Lung cancer	406	31.06	23.86

$p < 0.001$: between three group

$p1 < 0.001$: mesothelioma-breast cancer

$p2 < 0.001$: mesothelioma-lung cancer

$p3 = 0.095$: breast cancer-lung cancer

Table 3 Characteristics of residential area

Characteristics	*n*	%
Type of geologic rocks		
Guleman ophiolite (JKg)	11	11.8
Karadut complex (Kk)	58	62.4
Koçali Complex (JKk)	24	25.8
Position of residential area about asbestos source		
In source area	37	39.8
Out of source area	56	60.2
Distance of residential area from asbestosis area		
In source	37	39.8
Distance <10 km	34	36.6
Distance >10 km	22	23.6
Residential area angular location wind direction*		
(±) 30°	34	36.6
(±) 30°–60°	23	24.7
(±) 60°–90°	10	10.8
(±) 90°–120°	12	12.9
(±) 120°–150°	7	7.5
(±) 150°–180°	7	7.5

* Number and rate of the MM determined residential area that on both sides of the predominant wind direction from the central area of asbestos (±) 30°

Discussion

Environmental exposure to asbestos as a cause of mesothelioma has been well documented in many studies [16, 17]. In Turkey, many MM cases have been reported to result from environmental asbestos exposure [21–23].

In one study carried out in Diyarbakir, asbestos was found in several villages as the result of soil analysis [22, 24]. In that study, concentrations of asbestos in an active mine were found to be 4.9 fibers/cm^3, and that in a house that was plastered with asbestos was found to be 1.24 fibers/cm^3. In Turkey, the relationship of MM case frequency to the distance from the source and wind direction has not previously been studied. Additionally, this is the first study to investigate MM incidence in relation to geological factors in Turkey.

A major strength of our study was the very large number of MM cases used to assess the potentially weak association between exposures and asbestos sources.

In Turkey, Bayram et al. found a significant relationship between proximity to NOA areas and mesothelioma or pleural plaques. The risk of developing malignant mesothelioma or pleural plaques was halved by every additional 5 km distance of the birthplace from NOA [23]. Bayram et al. found having been born close to ophiolites was associated with a substantially increased risk of MM compared with breast and prostate cancer [23]. To our knowledge, the present study used a larger number of patients than did previous similar reports [23, 25].

Besides smoking, other risk factors for lung cancer are arsenic, particulates from diesel engine exhausts, radon, and exposure to asbestos and other mineral fibers [26]. We aimed to investigate relationship of distance of NOA for MM, lung cancer and breast cancer patients. Mean distance of mesothelioma 6.26 km, lung cancer 31.06 km, breast cancer 34.31 km (Table 2).

We found more MM cases than lung and breast cancer cases near areas of NOA. We found lung cancer near to NOA than breast cancer but this difference not statistically important.

Table 4 Asbestos mesothelioma incidence by type of rock

Type of rock	*n*	Mean incidence n/100.000	SD	*p*	*p*1	*p*2	*p*3
Guleman ophiolite (JKg)	11	1440.4	1733.3	**0.048**	**0.02**	0.71	**0.035**
Karadut complex (Kk)	58	336.7	301.9				
Koçali complex (JKk)	24	1086.9	2081.3				

Significant values are in bold

p anova test significant value

*p*1: JKg & Kk

*p*2: JKg & JKk

*p*3: JKk & Kk

SD standard derivation

Table 5 The incidence of mesothelioma by distance of asbestos contain area

Distance	*n* (residential area)	Mean incidence *n*/100.000	SD	*p*	*p*1	*p*2	*p*3
In asbestos area	37	1059.5	1891.4	**0.038**	0.15	**0.045**	0.731
<10 km from area	34	499.2	592.5				
>10 km from area	22	240.1	214.1				

Significant values are in bold

p anova test significant value

*p*1:asbestos area & <10 km

*p*2: asbestos area & >10 km

*p*3: < 10 km & >10 km

SD standard derivation

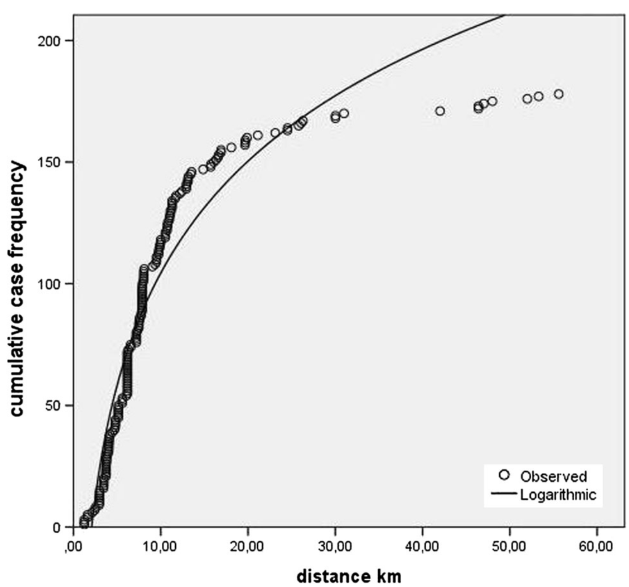

Fig. 4 Result of curve estimation model for MM

A cross-sectional study from Sivas, Turkey, reported an 8 % decrease in the risk of acute respiratory disease for every additional km of distance from ophiolites [25]. In another study in Turkey, asbestos-related diseases were higher among residents living closer to ophiolites [25]. Pan et al. examined the relationship between residential proximity to ultramafic rocks (rocks originating from the oceanic crust) and mesothelioma risk in the United States and found that the risk decreased by 6.3 % for every 10 km distance from the NOA source [15].

In those previous studies, only distance was investigated. We investigated distance, area of asbestos occurrence, and wind direction. Most of the MM cases were seen in or near asbestos-containing areas. Only 20 (23.6 %) patients were >10 km away from the source, and 10 (5.6 %) patients were >25.5 km away from the source.

One prior study of asbestosis and the effect of wind have been reported [20]. Wind direction is known to determine the concentration of asbestos fibers in specific areas, and asbestos concentrations in the air surrounding the emission point depend on wind direction and velocity [27].

One study has considered that meteorological factors could be related to pleural mesothelioma deaths by environmental exposure [16]. In that study, a significantly elevated standardized mortality ratio (SMR) was reported among persons who lived in the area with relatively high concentration levels. Furthermore, significantly elevated SMR was found as far as 2200 m south-southwest of the factory, the predominant wind direction, but only 900 m in the opposite, north-northeast direction. Therefore, a parameter that includes meteorological conditions is a better proxy for exposure dose than is residential distance alone, and it should be useful for a more accurate investigation of the effects of asbestos exposure among community residents [16].

In another study, the incidence of pleural mesothelioma was very high in the northeast and southeast quadrants of the 500-m sector coinciding with the study area's predominant wind directions [14].

We found the largest number of residential areas where MM cases occurred to be within ±30° of the predominant

Table 6 Factors predicting incidence of MM (linear logistic regression result)

	Unst. coeff B	Std. error	Std. coef beta	*t*	*p*	95.0 % CI for B
Constant	2.55	0.74		34.3	>0.001	2.41 to 2.70
Area * cos α	0.003	0.001	0.22	2.09	0.039	0.000 to 0.005
d^2	−0.001	0.000	−0.19	−1.89	0.062	−0.001 to 0.000

D^2 square of distance

wind direction (Table 3). The present study showed that the distance of a residence from a contaminating asbestos source and the predominant wind conditions in the area can influence the risk of developing environmental mesothelioma.

The Kk (Late Triassic–Late Cretaceous) is characterized by flysch and wildflysch containing clayey limestone with limestone, ophiolitic rocks, and cherty shale and limestone [17, 24]. We found the lowest MM incidence in Kk compared with the other two rock types (Table 4). This low incidence may be associated with the fact that Kk contains more deep-sea origin flysch and small amounts ophiolite [17, 24]. We believe that the type and content of rock affects MM incidence.

The matrix of JKg contains serpentinite, mudstones of varying color with radiolarites, cherts, shale, and volcanics, indicating Late Cretaceous rock [17, 24]. JKg contains greater amounts of ophiolite than does Kk.

The Guleman Ophiolite corresponds to the lower part of the oceanic lithosphere, including mantle tectonites and ultramafic to mafic cumulates. Isolated dikes cut through the aforementioned rocks at different structural levels. Mantle tectonites are more than 4 km thick and form at least 60 % of the whole ophiolite body [28, 29]. The Guleman Ophiolite contains serpentinized peridotite grading upward through a transition zone of alternating peridotite–pyroxenite with increasing amounts of gabbro into banded gabbro [30]. We found a high MM incidence in and near JKg areas. We believe the asbestos content of JKg is higher than that of Kk. Moreover, in one study in Diyarbakir, tremolite was found in rock analysis [22].

Bayram et al. found that MM incidence decreased with each 5 km of distance from NOA [23]. In the present study, 30 MM incidence decreased with each 10 km of distance from the asbestos-containing source ($p = 0.038$). High MM risk was found in residential areas located in or near NOA areas.

We defined a model to predict MM incidence. In this model, we calculated factors affecting MM incidence from asbestos-containing sources. In this model, the logarithmic incidence of MM increases 0.03 fold with each point increase in the value of area*cos α; in contrast, incidence decreased 0.01 fold with each point increase in the square of the distance from the source (Table 6).

One limitation of this study is that the duration of cumulative fiber exposure could not be estimated because we considered only the place of birth and not the entire residential or occupational history of the patients. Nevertheless, that the birthplace was demonstrated to be such a strong determinant of risk suggests that it is a good predictor of lifetime exposure and/or that early-life exposure to asbestos is crucial to determine the risk of later disease.

MM resulting from the use of NOA fibers for whitewashing houses has been shown in some areas. In some parts of the world, people are and will be at risk of exposure to NOA because of the geological properties of the place where they live.

MM was higher in areas near NOA and aligned with the dominant wind direction. In conclusion, MM incidence and risk are affected by geological and meteorological factors.

Detailed investigations are needed to further examine the influence of living close to ophiolites on the development of mesothelioma.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animal rights and informed consent All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Dicle University Ethics Committee obtained ethical approval.

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