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PLEURAL MESOTHELIOMA IN HOUSEHOLD MEMBERS OF ASBESTOS-EXPOSED WORKERS IN FRIULI VENEZIA GIULIA, ITALY

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Abstract

Objectives: Malignant mesothelioma is closely associated to asbestos exposure. One such exposure may occur through contact with occupationally exposed household members and their belongings. This study examines the features of pleural mesothelioma attributable only to asbestos brought home by another family member. **Material and Methods:** The data sources were 1063 mesothelioma cases diagnosed between 1995 and 2014, from the Friuli Venezia Giulia Mesothelioma Register. In all cases the diagnosis of mesothelioma was based on the pathology report. Exposure information and demographic data were acquired by an occupational medical standardized questionnaire/interview. **Results:** Household-exposure mesothelioma cases included 33 women and 2 men. Relationships were: wives (N = 22), daughters (N = 9), sons (N = 2), and mothers (N = 2). Asbestos exposure in the workers predominantly occurred in shipyards. Out of the 35 pleural cases, 19 were epithelial, 9 biphasic, 3 sarcomatoid, and 4 not specified. The mean age at diagnosis was 77 years old. The mean latency was 59 years, with wives having a significant shorter latency than offspring. Latency was not significantly related to morphology and asbestosis. The overall mean survival was 16 months (median 11 months) but treatment was beneficial (mean 16 months vs. 7 months). Biphasic/sarcomatoid histology and presence of asbestosis were associated with a decreased survival, although not with statistical significance. **Conclusions:** Our data confirms that household exposure increases the risk for pleural mesothelioma amongst women with no history of occupational asbestos exposure. This is an ongoing problem in many countries, as well as in Italy, where the evaluation of a framework for the compensation of these cases is under debate. Int J Occup Med Environ Health 2017;30(3):419–431

Key words: Latency time, Asbestos workers, Family members, Household exposure, Pleural mesothelioma, Mesothelioma register

INTRODUCTION

Mesothelioma is closely associated with asbestos exposure: a history of asbestos exposure may be found in > 80% of mesothelioma cases [1]. Mesothelioma may arise in various locations – most commonly the pleura and the peritoneum and only rarely other serosal surfaces. The great majority of asbestos-induced mesothelioma in the industrialized world is caused by the occupational asbestos exposure, and occurs among workers engaged in extracting and manufacturing asbestos, or performing tasks involving contact with asbestos-containing materials [2]. The concern used to be focused on the occupational environment

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but it is recognized that asbestos fibers are widely spread in the environment. People may be exposed to asbestos in various non-occupational circumstances: domestic exposure living with asbestos workers, with regular exposure to soiled work clothes brought home; environmental exposure in the neighborhood of industrial sources (asbestos mines and mills, asbestos processing plants); passive exposure in buildings containing asbestos; and natural environmental exposure to geological sources [3].

Individuals exposed in the non-occupational setting may have similar asbestos fiber lung burden to those exposed in the occupational setting, presenting a significant mesothelioma risk [4–6]. While exposure in non-occupational settings is generally much lower than the one in occupational circumstances, the levels may not be negligible. It is thus likely that lifelong cumulative exposure may have been as high as in some occupational settings, but it was not, or not adequately, measured [7].

One such exposure, recognized since 1965 by Newhouse and Thompson [8], is asbestos brought home to family members on the hair, clothing and personal effects of asbestos workers. The increased risk for death from pleural mesothelioma amongst wives of asbestos-industry workers is well known from many international case-reports [4,6,9]. The risk of pleural mesothelioma in household members has also been investigated in several case-control [10] and cohort studies [11–13]. Between 1993 and 2012 a case-list of 21 463 malignant mesothelioma (MM) was recorded by the Italian National Mesothelioma Register (ReNaM) [14] and the modalities of exposure to asbestos fibers have been investigated for 16 511 (76.9%) of them, identifying 786 (4.8%) cases with a family exposure. Among the 786 mesothelioma subjects (675 women and 111 men), 738 were pleural and 47 peritoneal cases [14].

The ReNaM has a regional structure with the Operative Regional Centers (CORs) that actively research cases and classify asbestos exposure, according to the National Guidelines [15]. Since 1995, the Friuli Venezia Giulia Mesothelioma Register, included in the network of the ReNaM, has recorded the incident cases of the MM in the Region, an industrial area in Northeastern Italy with a history of extensive occupational asbestos exposure, mainly due to the existence of several shipyards in the Trieste-Monfalcone district.

This study examines the available residential and familial history and occupational and clinical data of individuals diagnosed with malignant mesothelioma, attributable only to asbestos brought home by another family member, from the Friuli Venezia Giulia Mesothelioma Register.

MATERIAL AND METHODS

The analysis is designed as a retrospective population-based study to identify mesothelioma cases in household members (e.g., wives, daughters/sons, sisters/brothers) of asbestos-exposed workers. The data sources are 1063 MM cases, available from 1995 to 2014, from the Friuli Venezia Giulia Mesothelioma Register.

The Friuli Venezia Giulia COR collects incident malignant mesothelioma cases from health care institutions that diagnose and treat cases of mesothelioma (especially pathology and histology units, pneumology and chest surgery wards), consults hospital discharge records and death certificates, analyzes the pathology diagnosis and classifies cases according to diagnostic certainty achieved (defined MM, probable MM, possible MM) [15].

Data on occupational and residential history together with lifestyle habits is reported directly from the subjects or their relatives using a standardized questionnaire/interview administered by an occupational physician.

Exposure to asbestos is classified as occupational (certain, probable, possible), household (when patients have lived with a cohabitant occupationally exposed), environmental (residence near a source of asbestos pollution without work-related exposure), hobbies (other non-occupational exposures like those due to leisure time activities), unlikely

or unknown (e.g., questionnaires reported an incomplete job and/or residential and familial history) following the National Guidelines [15,16]. Certain occupational exposure is attributed to the subjects whose work has involved the use of asbestos or materials containing asbestos; probable occupational exposure to the subjects who have worked in a firm where asbestos has been certainly used but whose exposure cannot be documented; possible occupational exposure to the subjects who have worked in a firm referring to an economic sector where asbestos has been used [15,16].

Exposure information and medical data were reviewed (by occupational physicians) in all cases included for the analysis. The diagnosis of mesothelioma was based on the pathology report including immunohistochemical staining documenting the presence and location of mesothelioma. Demographic data, such as gender, age, age at 1st domestic exposure to asbestos, occupational history, and personal and family health history were collected and archived from the questionnaire/interview. In addition, general information of occupation, industry setting and the decade(s) of exposure of household contacts was acquired from this source. For each mesothelioma case, data on asbestos bodies, pleural plaques and asbestosis at autopsy, when performed, was recorded. The presence of asbestos-related disease in asbestos-exposed workers was also recorded, whenever available. There was no information available about measurements of quantitative asbestos fiber burden of lung tissue for any of the subjects in this study.

The latency period was defined as the time between the year of 1st exposure and the year of diagnosis. For wives or offspring the period of domestic exposure was estimated according to the period during which their husbands or fathers were occupationally exposed. For each wife, it was estimated that exposure began either the date of marriage or the date the husband was hired, whichever was later. The end of exposure was considered to be when the husband quit his job or the marriage ended, whichever it came earlier. For the wives who also had father occupationally exposed, the date of 1st household exposure to asbestos was taken to be the date of 1st exposure as recorded on the questionnaire/interview. The year of 1st exposure and age at 1st exposure were derived from the date of 1st exposure as defined above. Duration of exposure was calculated from the date of 1st exposure to the date of last exposure. Survival in months was calculated from the date of mesothelioma diagnosis or symptoms (if the former was not available) to the date of death. The closing date was set on December 31, 2014.

Difference in latency and survival between wives and offspring were assessed by the Chi^2 test. The survival data was also analyzed based upon parameters such as treatment modality, histological type and presence/absence of asbestosis. Statistical significance was defined as a p value < 0.05. All statistical analyses have been carried out by means of the SPSS software (version 20.0).

RESULTS

Between 1995 and 2014 among the 1063 cases (890 males, 173 females) recorded in the Friuli Venezia Giulia Mesothelioma Register, 50 cases were diagnosed amongst members of households where at least 1 worker had been occupationally exposed to asbestos. Among these cases, 15 (11 men and 4 women) who had worked for a period in industrial activities with certain (N = 9), probable (N = 3) and possible (N = 3) exposure to asbestos, were not included for this study. This resulted in a study group of 35 individuals.

Among the 35 mesothelioma cases that met inclusion criteria, 33 (94%) were female and 2 (6%) were male. Detailed job histories revealed that neither the women nor the men had ever worked in an asbestos industry sector. Their exposure was only through residential inhalation of asbestos from husband's or father's contaminated work clothes that were not removed in the workplace for cleaning but

were rather taken home, where the wives and/or daughters brushed and hand-washed them almost once a week.

Demographic and clinical data of the study group are reported in the Table 1. Mesothelioma cases are ordered by the date of diagnosis. In all cases the tumor site was the pleura, with a right-sided predominance (54%). Histological type was epithelial in 19 (54%) cases, biphasic in 9 (26%), sarcomatoid in 3 (9%), and not specified in 4 (11%) cases. The diagnosis was based upon tissue biopsy in 22 (63%) cases, cytological examination in 2 (6%) and autopsy in 11 (31%) cases. Among the 35 mesothelioma subjects, 22 (63%) underwent post-mortem examination. Diagnosis was confirmed by immunohistochemical reactions in 34 cases.

Mean age at diagnosis was 77±10 years old (the range of 50–93 years old). The age at diagnosis for offspring was slightly younger than for wives (73 vs. 78 years old), but this difference was not statistically significant. Out of those with available smoking data, there were 15 (75%) non-smokers and 5 (25%) smokers or ex-smokers.

In our study all cases of mesothelioma lived in the same household as the exposed worker(s). In the 7 cases of dual relationship (daughter and wife (N = 4), wife and mother (N = 2), daughter and sister (N = 1)) and in the only case of triple relationship (daughter, sister and wife), the earlier exposure is counted. Relationships were: wives (N = 22), daughters (N = 9), sons (N = 2), mothers (N = 2).

The Table 2 shows the distribution of industries and occupations in which asbestos exposure took place. The exposure setting with the highest number of workers who lived with the presented cases was a shipyard (possibly due to our location in the Trieste-Monfalcone ship-building and repair district), followed by maritime transport, engine construction, refinery, power generation, construction and firefighters. Unskilled workers and welders were the most commonly identified occupations. Some family members worked in and were consequently registered in > 1 industry and/or occupation, which resulted in a higher number of observations than family members (N = 44).

Our series includes individuals with household asbestos exposure from 1920 up to 1992. The age at 1st exposure was < 10 years old in 11 cases, 10–19 years old in 4 cases, 20–29 years old in 16 cases, ≥ 30 years old in 4 cases. The mean age at 1st exposure in the study group as a whole was 18±13 years old, while in the case of wives it was 26±7 years old. On average, wives had a slightly shorter duration of exposure than offspring (23.3 years vs. 27.9 years), but this difference was not statistically significant.

Out of the 22 cases with available data about other asbestos-related disease, asbestosis was present in 7 cases. Among these, 3 had pleural plaques as well. Asbestos bodies were observed on routine lung sections in 4 cases. Pleural plaques (N = 4), asbestosis (N = 4), lung cancer (N = 2) and mesothelioma (N = 1) were also reported for 8 husbands and 1 father occupationally exposed. The husbands as well as the father were employed in a shipyard.

In this study the mean latency was 59±15 years. Wives did have the shorter latency period than offspring (53 years vs. 73 years, $p < 0.05$). The latency period was not significantly related to morphology: no statistical difference was found in the latency for epithelioid versus biphasic/sarcomatoid and not specified tumors (57 years vs. 63 years and 55 years, respectively). Furthermore, there was no statistical difference in latency comparing those with (N = 7) and without (N = 15) asbestosis (67 years vs. 59 years, respectively).

Among the 35 cases of mesothelioma reviewed in this series, 13 underwent some sort of treatment: decortication/pleurectomy in 8 cases and a combination of systemic chemotherapy and radiation therapy in the remaining cases. Most (63%) of the mesothelioma cases were not treated, apart from palliative care.

At the end of the study (December 31, 2014), 97% of the subjects died (only 1 woman, a wife, was alive). The overall median of survival was 11 months. There was

Table 1. Demographic data, pathology and exposure of household member mesothelioma cases (N = 35) diagnosed between 1995 and 2014

Patient No.	Relationship	Year of birth	Histological type	Diagnosis		Year of death	S.t.d. [months]	Autopsy findings	Patient age at 1st exposure [years]	Latency [years]	Exposure [years]
				year	patient age						
1	wife	1910	NOS	1996	86	1996	1	NSF	25	61	32
2	daughter, wife	1928	epithelial	1998	70	1999	14	NA	birth	70	41
3	wife	1919	mixed	1998	79	1998	2	asbestosis, pleural plaques	22	57	29
4	wife	1912	epithelial	1999	87	1999	1	asbestosis, pleural plaques	36	51	21
5	son	1924	sarcomatoid	1999	75	2000	5	NSF	birth	75	20
6	wife	1912	NOS	2000	88	2000	2	NSF	22	66	36
7	wife	1911	epithelial	2000	89	2000	3	LAB	29	60	20
8	wife	1937	epithelial	2000	63	2001	16	pleural plaques	23	40	28
9	daughter, sister, wife	1942	epithelial	2000	58	2001	9	asbestosis	birth	58	36
10	wife	1931	mixed	2002	71	2005	52	pleural plaques, LAB	27	44	12
11	mother	1932	mixed	2002	70	2002	9	NA	40	30	7
12	wife	1930	NOS	2002	72	2004	21	NSF	26	46	4
13	wife	1953	epithelial	2003	50	2004	62	NSF	19	31	20
14	daughter, wife	1920	epithelial	2004	84	2006	31	NSF	birth	84	66
15	wife	1924	epithelial	2004	80	2006	19	NA	23	57	31
16	wife	1934	epithelial	2005	71	2006	11	NA	46	25	10
17	wife	1932	epithelial	2005	73	2006	12	NA	22	51	29
18	wife, mother	1914	sarcomatoid	2006	92	2006	4	asbestosis	18	74	28
19	daughter, wife	1932	mixed	2006	74	2006	15	asbestosis, LAB	birth	74	56
20	daughter, wife	1940	epithelial	2006	66	2009	41	NA	birth	66	40
21	wife	1929	NOS	2006	77	2008	58	NA	32	45	20
22	daughter	1944	mixed	2007	63	2009	18	NA	birth	63	20
23	wife	1939	epithelial	2007	68	2008	19	LAB	21	47	19
24	wife	1927	epithelial	2007	80	2007	2	NA	28	52	17

Table 1. Demographic data, pathology and exposure of household member mesothelioma cases (N = 35) diagnosed between 1995 and 2014 – cont.

Patient No.	Relationship	Year of birth	Histological type	Diagnosis		Year of death	S.t.d. [months]	Autopsy findings	Patient age at 1st exposure [years]	Latency [years]	Exposure [years]
				year	patient age						
25	wife	1929	epithelial	2008	79	2011	32	NA	20	59	39
26	daughter	1931	epithelial	2009	78	2010	8	NSF	birth	78	37
27	wife	1930	epithelial	2010	80	2011	15	NA	17	63	33
28	wife	1926	sarcomatoid	2010	84	2010	7	pleural plaques, LAB	22	62	25
29	mother	1923	mixed	2011	88	2011	0	asbestosis	23	65	25
30	wife	1929	epithelial	2011	82	2013	20	pleural plaques	26	56	20
31	daughter, sister	1921	mixed	2012	91	2012	2	asbestosis, pleural plaques	birth	91	27
32	daughter	1935	epithelial	2012	77	2013	22	NA	birth	77	2
33	wife, mother	1920	mixed	2013	93	2013	0	NSF	27	66	22
34	son	1949	epithelial	2014	65	2014	4	NSF	birth	65	2
35	wife	1937	mixed	2014	77	alive	> 6	NA	19	58	32

S.t.d. – period from symptoms onset to death; NOS – not otherwise specified; NFS – no specific finding; NA – not available; LAB – lung asbestos bodies.

Table 2. Exposure in household member mesothelioma cases (N = 35) diagnosed between 1995 and 2014 and in occupationally exposed family members

Patient No.	Period of household exposure	Family member	Industry sector	Occupation	Work beginning [year]	Work quitting [year]
1	1935–1967	husband	shipbuilding	painter	1920	1967
2	1928–1969	father	shipbuilding	unskilled worker	1928	1956
		husband	shipbuilding	wrecker	1956	1969
3	1941–1970	husband	shipbuilding	ironworker	1930	1970
4	1948–1969	husband	shipbuilding	carpenter	1948	1969
5	1924–1944	father	shipbuilding	unskilled worker	1924	1944
6	1934–1970	husband	shipbuilding	welder	1925	1970
7	1940–1960	husband	engine construction	boilermaker	1940	1960

8	1960–1988	husband	shipbuilding	welder	1951	1988
9	1942–1978	father	shipbuilding	unskilled worker	1937	1973
		brother	shipbuilding	welder	1956	1961
		husband	shipbuilding	welder	1963	1978
10	1958–1970	husband	shipbuilding	carpenter	1958	1970
11	1972–1979	son	shipbuilding	welder	1972	1992
12	1956–1960	husband	construction	unskilled worker	1956	1958
			shipbuilding	insulation installer	1958	1960
13	1972–1992	husband	shipbuilding	welder	1968	1992
14	1920–1986	father	shipbuilding	unskilled worker	1920	1946
		husband	shipbuilding	mechanic	1945	1986
15	1947–1978	husband	shipbuilding	unskilled worker	1937	1942
			refinery	unskilled worker	1947	1978
16	1980–1990	husband	shipbuilding	unskilled worker	1961	1990
17	1954–1983	husband	shipbuilding	welder	1947	1983
18	1932–1960	husband	shipbuilding	carpenter	1932	1957
		son	shipbuilding	cable duct maker	1947	1960
19	1932–1988	father	shipbuilding	unskilled worker	1932	1956
		husband	firefighters	firefighter	1956	1988
20	1940–1980	father	shipbuilding	electrician	1935	1970
		husband	shipbuilding	ironworker	1955	1980
21	1961–1981	husband	shipbuilding	ironworker	1948	1981
22	1944–1964	father	shipbuilding	ironworker	1944	1964
23	1960–1979	husband	shipbuilding	mechanic	1944	1989
24	1955–1972	husband	shipbuilding	ironworker	1955	1972
25	1949–1988	husband	shipbuilding	welder	1943	1988
26	1931–1968	father	shipbuilding	mechanic	1930	1968
27	1947–1980	husband	shipbuilding	lathe operator	1941	1980
28	1948–1973	husband	shipbuilding	lathe operator	1948	1973
29	1946–1971	son	refinery	repairman	1946	n.a.
			shipbuilding	mechanic	n.a.	1971

Table 2. Exposure in household member mesothelioma cases (N = 35) diagnosed between 1995 and 2014 and in occupationally exposed family members – cont.

Patient No.	Period of household exposure	Family member	Industry sector	Occupation	Work beginning [year]	Work quitting [year]
30	1955–1975	husband	maritime transport	repairman	1955	1975
31	1921–1948	father	power generation	stocker	1921	1948
		brother	engine construction	lathe operator	1938	1948
32	1935–1937	father	shipbuilding	unskilled worker	1935	1937
33	1947–1969	husband	shipbuilding	welder	1947	1969
		son	shipbuilding	electrician	1962	1966
34	1949–1951	father	shipbuilding	unskilled worker	1949	1951
35	1956–1988	husband	maritime transport	electrician	1953	1988

n.a. – not available.

no statistical difference in survival between wives and offspring. In examining the 3 histological types for prognostic differences, a significant survival benefit for epithelioid versus biphasic/sarcomatoid and not specified tumors (mean 13 months vs. 6 months and 12 months, respectively) was not found. Comparing those with and without asbestosis, a shorter survival was found in those with asbestosis (mean 5 months vs. 17 months), but this difference was not statistically significant. There was a statistically significant difference comparing survival time with and without treatment (mean 16 months vs. 7 months, $p < 0.05$).

DISCUSSION

Emerging data about pathophysiology of mesothelioma suggests that non-occupational and occupational asbestos exposure are non-differentiating variables with regard to causality [4,17,18]. These studies demonstrate that the occupational as well as non-occupational exposure may be anything from very heavy to very low. The family of an asbestos worker, for example, could be exposed to considerable amounts of asbestos brought home on his working clothes, and it was often the case that it was the duty of the wife or daughter to clean the clothes [19]. Thus, the fiber concentrations in domestic exposure might be as high as in the occupational setting. Nicholson et al. [20] found that chrysotile asbestos concentrations in the air of the homes of 13 asbestos mine and mill employees ranged from 50 μg/m^3 to > 2000 μg/m^3. Samples from 3 neighboring homes of non-miners ranged 32–65 μg/m^3. Brushing clothes might give peaks of > 100 fibers/ml, which may remain in the house for years and be airborne again whenever disturbed [21].

Thus, the typical non-occupational exposure is low or very low, but occasional high exposure occurs when there is a disturbance of some kind [17]. Moreover, while fiber dose may be lower in the non-occupational settings, the duration of exposure may be much longer in the non-occupational as compared with the occupational setting

because the asbestos fibers permeate the environment. Therefore, cumulative exposure may be comparable between occupational and non-occupational cases [18]. Huncharek et al. [22] reported that the lung asbestos fiber content of a shipyard machinist's wife was similar to that seen in cases of mesothelioma associated with the occupational exposure. Bianchi et al. [23] found asbestos bodies in 6 asbestos workers' wives with only household exposure. Between 1000 and 10 000 asbestos bodies/g of dry lung tissue were measured in the half of the wives; as many as 10 000–100 000 asbestos bodies/g of dry lung tissue were reported in the case of 1 wife. Such concentrations are comparable to those found amongst 56 shipyard workers.

Evidence of mesothelioma for wives of asbestos-industry workers has been recognized since the date of the report of Newhouse and Thompson [8] which included 7 mesothelioma cases that had washed the work clothes of their occupationally exposed husbands and siblings. In a cohort study, Ferrante et al. [13] showed a statistically significant increase in both pleural cancer mortality and pleural mesothelioma incidence among women who had been exposed to asbestos at home as wives of asbestos-cement workers.

Other reports show that not only wives but also sons and daughters are at risk from asbestos brought home by exposed workers. In the Anderson cohort study on amosite workers, 3 cases of mesothelioma had been exposed to asbestos at home during their childhood [11]. Kane et al. [19] reported 5 cases of pleural mesothelioma < 40 years attributable to household exposure during childhood, exclusively through their fathers, most of whom were working in the shipyard industry. Roggli et al. [24] found that 33 out of 59 female mesothelioma cases with an available exposure history were family contact only. A previous study on family mesothelioma in the Trieste-Monfalcone ship-building and repair district reported 5 patients who had been exposed at home while washing asbestos-contaminated work clothes [9]. A study carried out in the United States reported 32 household-exposure mesothelioma cases from relatives employed in asbestos-associated industries [6].

The 32 household-exposure cases in the Miller [6] series were similar to the said series in the distribution of tumor location (27 pleural vs. 5 peritoneal mesotheliomas) and histological type (17 epithelial, 9 fibrous/biphasic, and 6 not specified), frequency of pleural plaques and asbestosis (10 cases and 4 cases, respectively), distribution of family relationships (15 wives, 11 daughters, 3 sons, 1 sister-in-law, 1 niece, and 1 boarder) and exposure setting of household contacts (shipyard was the main industry sector with the highest number of exposed family members). In our study the ship-building and repair industry, in which asbestos primarily had been used for insulation purposes, also accounted for the largest part of asbestos exposures.

Household exposure has been suggested as the source for mesothelioma presenting at an earlier age [19]. In this study the mean age at diagnosis was 77 years old. The fact that 80% of our cases were ≥ 70 years old shows that household exposure should not be ruled out when mesothelioma is detected in an older individual. The majority of mesothelioma cases (90%) among men are attributable to asbestos and are pleural [25], in contrast only 20% of mesotheliomas among women are recognized as asbestos-related and 2/3 are pleural [26]. In this series, all cases were pleural and 33 occurred in women (predominantly wives). Moreover, asbestosis and pleural plaques were noted in 32% of those with available data. The presence of asbestosis, pleural plaques, and asbestos bodies also correlated with asbestos exposure.

Seven women had developed asbestosis. Asbestosis most commonly occurs among men following prolonged and usually heavy occupational exposure to asbestos. The presence of asbestosis among women with non-occupational asbestos exposure is a relevant aspect of this study, seldom reported in the literature [6]. In all patients the diagnosis, based on radiological features, was always

confirmed by histology on lung tissue specimens obtained from autopsy; therefore among these patients the risk of misclassification should be negligible. All the patients with asbestosis had never worked in an asbestos industry: asbestos exposure was attributable exclusively to asbestos brought home by another resident of the household. The husbands of 2 women had also developed pulmonary asbestosis, and the father of 1 patient died of lung cancer. Between 1930 and 1973, both the husbands and the father were employed in a shipyard in the Trieste-Monfalcone district. The severity of asbestos exposure in the shipbuilding and maintenance industry as well as the high incidence of pleural mesotheliomas in the shipyard areas has been well documented [9].

The prolonged latency period (59 years) found in the current study is consistent with other studies [16,27]. Marinaccio et al. [16] reported the mean latency of 48 years among household exposed mesothelioma cases which was significantly longer than that of 43 years observed among the occupationally exposed ones. As hypothesized in a recent study, it is possible that women, who have a longer latency than men, tend to have lower exposures than men due to their mainly non-occupational asbestos exposure [27]. In this study there has been a female preponderance and the source of exposure has been non-occupational, so this could be an explanation for our results.

Wives had a significant shorter latency than offspring, despite similar duration of exposure. This may be consistent with a greater burden of asbestos wives.

This study has revealed no statistical difference in latency comparing those with asbestosis (who, presumably, had greater exposure) and without. This finding would seem contrary to the opinion that the heavier the asbestos exposure, the shorter the latency, nevertheless other researchers have reported similar results [27].

It is necessary to underline that it is particularly complex to identify the start of asbestos exposure for mesothelioma cases of non-occupational origin. In this analysis, the 1st year of cohabitation (or the year of 1st exposure beginning for the cohabitant) was considered as the onset of asbestos exposure [16]. For example, for each wife, the time of 1st exposure to asbestos was considered to have coincided with the date of marriage or the date the husband was hired, whichever was later. As a matter of fact, the beginning of a work period could not exactly correspond to the beginning of exposure to asbestos and it could lead to an overestimation of latency time [16].

As stated in the epidemiological literature [16], the retrospective analysis of collected cases – as usual for an incidence surveillance system – could "miss" the cases with the shorter latency thereby overestimating the mean latency period. In addition, the possible presence of competitive causes of death (e.g., asbestos related lung cancer and asbestosis) and the incomplete cohort analysis (our study population comprised cases collected in recent years and, hence, cases with relevant past exposure and short latency could be missing) induce a possible bias in the statistical inference about differences in latency.

The survival from malignant mesothelioma has been poor. Our results (median survival of 11 months, mean survival of 16 months) are consistent with survival values reported by other studies. The reported range for median survival for pleural mesothelioma in a 2009 review, regardless of stage, was 9–17 months [28]. In many studies, epithelial histology is associated with a better prognosis than the biphasic or sarcomatoid type [27]. Our study has found a longer survival for epithelial histology compared to biphasic/sarcomatoid type but this difference was not statistically significant. Comparing those with and without asbestosis, our data – as it would be expected – has revealed a longer survival for those without asbestosis but this difference has not reached statistical significance.

Results are conflicting about the survival in patients treated with combinations of therapies as compared to patients receiving only palliative treatment. In some

studies an effect on prognosis of combinations of therapies compared to only palliative treatment has been observed [27,29], while others have reported no effect [30]. A case series of 238 pleural and peritoneal mesotheliomas reported a mean survival of 11.3 months for patients receiving therapy vs. 6.4 months in those that remained untreated [27]. Our results show a statistically significant improvement in survival with treatment. Unfortunately, many patients with mesothelioma are often diagnosed at a late stage. Thus, these patients may benefit less from therapies because of advanced diseases, highlighting the role of asbestos exposure history in early diagnosis [29].

CONCLUSIONS

Non-occupational subjects are more likely to be underrecognized than those with occupational exposure because of recall and gender bias. Given the long latency period involved, such exposure may be rather remote and involve poor recollection [27].

However, the predominance of women in the household contact cases and the long latency of asbestos-induced diseases underline the importance of collecting a detailed exposure history of mesothelioma subjects who claim to have had no occupational asbestos exposure. These patients should trigger a suspicion of secondary asbestos exposure through household contact [31]. Such exposure may have taken place in the great number of women whose mesotheliomas have not been attributed to asbestos.

The current study confirms the increased risk of pleural mesothelioma from domestic exposure for relatives of occupationally exposed workers. This is an ongoing problem in many countries, as well as in Italy, where the issue of insurance and welfare protection for mesothelioma cases related to non-occupational asbestos exposure is under debate. The evaluation of a framework for the compensation of these mesothelioma cases needs to be carefully undertaken from economic, ethical and insurance points of view [32].

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