

Incidence of pleural mesothelioma in Liguria Region, Italy (1996–2002)

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Abstract

In this study, incidence of pleural malignant mesothelioma (PMM) in the Liguria Region (Italy) (approximately 1.6 million inhabitants), in the presence of asbestos exposure was investigated.

New PMM cases recorded by the Mesothelioma Registry of Liguria, from 1996 to 2002 and interviews reported on a standardised questionnaire were analysed according to demographical and etiological characteristics. Nine hundred and forty five PMM cases were recorded (757 males and 188 females); the age standardised (European population) incidence rates per 100000 were 8.51 and 1.43, respectively. The rates among the four provinces ranged between 1.18 and 13.7 for males and 0.68 and 1.44 for females. The questionnaire was evaluated for 786 PMM cases (or next-of-kin). Higher incidence rates were reported in the provinces with larger industrial and harbour areas, including shipyards (construction and repair), dockyards, building activities, chemical and heavy industrial activities. Asbestos exposure was unlikely or unknown for 57.5% females and 15% males. A major role of environmental asbestos exposure in the etiology of PMM is hypothesised for females and for a minor proportion of males.

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1. Introduction

Malignant mesothelioma (MM) is a highly lethal tumour that arises in the pleura and peritoneum, but cases have been also reported in the pericardium and in the tunica vaginalis testis. Formerly rare, its incidence is increasing throughout the industrialised world and it is quite generally associated with past exposure to asbestos which is the main known risk factor [1–5].

In industrialised countries where asbestos was used widely, incidence rates are about 1–2 per 1000000 per year among women and about 10–30 per 1000000 per year among men [6–9]. Incidence rates are increasing in most parts of Europe, even if the rate has decelerated in some countries [10]. In France, an estimated range of about 800–1600 males are anticipated to die annually by the year 2030 [11,12]. In the United Kingdom, incidence rates are expected to peak in the year 2020 at about 2700–3300 male deaths per year and then to decline rapidly thereafter [13]. Similar patterns were anticipated for other European countries [14], but, according to recent updates, the incidence

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peaks might now be anticipated between 2003 and 2013 [15,16], depending on the different countries. In Italy, the likely peak period of 800 annual male mesothelioma deaths from asbestos has been predicted to be between 2012 and 2024 [17].

Average latency period is commonly accepted to be 30–40 years [18,19], but shorter as well as longer latency periods have been observed. Cases diagnosed 60 years after the first occupational exposure have been reported [20]. Therefore, even if asbestos use was banned at different time points in many countries all over the world, it will likely be a public health problem in the future for developing countries.

The considerations traced above and the fact that Liguria region is the area with the highest mortality and incidence rates from MM in Italy [21–23] led to the activity of the Mesothelioma Registry of Liguria in 1994, which was developed as a Regional Operating Center (COR) of the National Mesothelioma Registry (ReNaM) [24].

Liguria COR is a population-based cancer registry specialised in the study of incidence, etiology and survival analysis of primary pleural and peritoneal MM cases in Liguria (Italy). Aims of the COR are the collection of demographic (including amongst other gender, birth date, residential address and death date); clinical (anamnesis, diagnosis, medical reports, microscopic and immuno-cytohistochemical evaluations, X-rays and computerised axial tomography evaluations, cause of death); and etiological (living and working history, occupational and non-occupational exposure to asbestos, smoking habits) data on all the new cases diagnosed among the population resident in the Liguria region. COR's role also included calculation of incidence rates; analysis of survival data; and the evaluation of the role of asbestos and other exposures in the etiology of this malignant neoplasia. Analysis of incidence and etiology data about pleural malignant mesothelioma (PMM) cases collected during the period 1996–2002 are reported in this paper.

2. Patients and methods

Since 1996 the Mesothelioma Registry of Liguria (COR) has been recording all new PMM cases diagnosed in the entire Liguria Region. This region is divided into four provinces (from west to east): Imperia (IM, ≈205 200 inhabitants), Savona (SV, ≈272 500 inhabitants), Genoa (GE, ≈878 000 inhabitants), La Spezia (SP, ≈215 900 inhabitants) [25].

All new cases were brought to COR's attention by personnel of the Regional and National Health Care Service, and a computerised Hospital Admission Records permitted the evaluation and improvement of data quality and completeness.

ReNaM reference diagnostic protocols were used to standardise the diagnostic criteria for MM, and cases were classified as certified, probable, and possible depending on the level of diagnostic certainty achieved [24].

In addition to clinical information, COR also collected standard occupational and environmental data in order to identify working and living areas at risk for asbestos-related pathologies.

All the subjects included in the COR database were invited to an interview and a standardised questionnaire was completed; when a subject could not answer, next-of-kin were invited. The questionnaire investigated principally the residential and occupational history with exposure assessment; exposure of relatives; presence of indoor asbestos objects; probable sources of environmental pollution; exposure to X-rays; previous respiratory pathologies; and smoking habits.

The cases analysed in the present study were diagnosed in the period 1996–2002.

Annual age specific rates for 100 000 inhabitants; crude rates for 100 000 inhabitants; and age standardised rates (ASR) for 100 000 inhabitants (European standard) were calculated and compared. Geographical comparisons were performed estimating the standardised rate ratio (SRR) using Imperia province, the area with the lowest proportion of subjects involved in asbestos-related activities, as a reference [26].

3. Results

3.1. Analysis of incidence data

In the period from 1996 to 2002, COR recorded 945 incident cases diagnosed as a certified, probable or possible PMM. Seven hundred and fifty seven (80.1%) cases were males and 188 (19.9%) were females. The mean age at diagnosis was 71.2 for males (range 34.8–97.2), and 74 for females (range 41.4–98.4).

When cases and ASR by gender was compared by year of diagnosis, rates appeared progressively increasing among males and a slight reduction among females (Table 1). The highest ASR was recorded in the province of La Spezia (13.7) for males and in the province of Genoa (1.4) for females (Fig. 1). Epithelial PMM was the most frequent morphological type (66.1%), followed by fibrous (10.1%), biphasic (9.3%) and desmoplastic (0.5%) types. According to gender, the frequency of epithelial cases was higher among females (73.8%) than among males (64.5%); while on the contrary, fibrous type accounted for 11% and 5.6% of the cases among males and females, respectively (Table 2). Age specific incidence rates showed a similar trend in the four provinces among males, while the reduced number of cases

Table 1

Incident cases, age standardised rate (ASR, Europe std.) and its standard error (SE), of pleural malignant mesothelioma in Liguria, between 1996 and 2002, by gender and year

Year	Males				Females			
	Cases	%	ASR	SE	Cases	%	ASR	SE
1996	92	12.1	7.53	0.82	28	14.9	1.45	0.31
1997	105	13.9	8.41	0.85	24	12.8	1.51	0.35
1998	102	13.5	8.12	0.83	27	14.4	1.59	0.34
1999	114	15	8.76	0.84	28	14.9	1.47	0.3
2000	105	13.9	8.33	0.84	26	13.8	1.33	0.29
2001	115	15.2	8.96	0.86	29	15.4	1.44	0.31
2002	124	16.4	9.29	0.87	26	13.8	1.28	0.29
Total	757	100	8.48	0.32	188	100	1.44	0.12

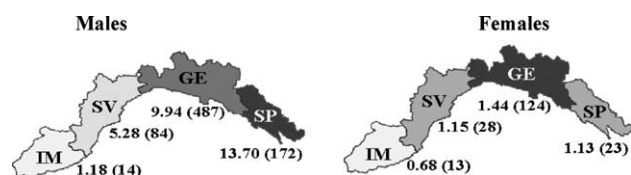


Fig. 1. Age standardised rates, Europe std. (number of cases) of pleural malignant mesothelioma in Liguria, by gender and four provinces Imperia-IM, Savona-SV, Genoa-GE, La Spezia-SP (1996–2002).

Table 2

Morphological characteristics

Morphology	Males		Females		Total	
	Cases	%	Cases	%	Cases	%
Epithelial	327	64.5	79	73.8	406	66.1
Fibrous	56	11	6	5.6	62	10.1
Biphasic	49	9.7	8	7.5	57	9.3
Desmoplastic	3	0.6	0	0	3	0.5
NoS ^a Malignant mesothelioma	72	14.2	14	13.1	86	14
Total	507	100	107	100	614	100
Morphology not available	250	33	81	43.1	331	35
Total	757	100	188	100	945	100

^a NoS: Not otherwise Specified.

among females did not permit the identification of a clear pattern (Fig. 2).

3.2. Analysis of etiological data

Details of exposure experienced by PMM cases were collected from 786 standardised questionnaires (341 (43.4%) interviewed the subject, 395 (50.2%) interviewed the next-of-kin). For remaining 50 subjects (6.4%), information were collected from hospital clinical records or other sources (Table 3). An occupational exposure (certified, probable, or possible) was identified in 83.7% of males against only 15.7% of females. A non-occupational exposure was detected for 1.3% of males,

while 26.8% of females experienced this kind of asbestos exposure. Then, non-occupational exposures (household (19.2%), environmental (6.2%)) appeared to be particularly frequent among females. The distribution of occupational exposure in each province among males was similar to that observed for PMM incidence rates: in fact, it ranged down from 91.5% of males occupationally exposed in La Spezia to 45.4% in Imperia. A clear pattern was not detectable among females, while approximately the same number of cases with unknown exposure was observed among males and females in each province and in the whole region, suggesting similar (but undetermined) environmental exposure levels. In fact, for 14.5% of males and 53.4% of females it was not possible to establish exposure status, since asbestos exposure was unknown from the incomplete information or data not available (see note in Table 3).

4. Discussion

According to currently available data and projections for the future, PMM incidence and mortality rates experienced in Italy, especially in some areas, are amongst the highest observed in Europe and in the world [23,27,28]. The present study has confirmed the high PMM incidence in Liguria region with a slight increase in male incidence rates during the observed period (1996–2002). Although time trends could have been influenced by different variables, such as PMM under-reporting [29] or misdiagnosis that likely occurred in the past [17], it appears unlikely that these factors could have affected such a recent set of data. In support of this point, major reviews have confirmed that the main cause of the recent increase of PMM among countries is due to occupational exposure to asbestos in previous decades [6,9,17,29,30].

The distribution of incidence rates observed especially among males does confirm the geographical relationship between concentration of industrial activities involving asbestos use and mesothelioma occurrence [23]. In fact, the province of Genoa provided the greatest number of cases (487), as it was the most populated province, but La Spezia showed the highest SRR (11.61) among males, when Imperia was used as a reference. As mentioned, Liguria is divided into four provinces (from west to east): Imperia, Savona, Genoa, La Spezia. Imperia is essentially characterised by rural and tourist activities; the same holds true for Savona, with the exception of a single, extensive, industrial site (prevalently chemical and carbon thermoelectrical plants) and an active commercial harbour. Genoa and La Spezia have a number of industrial activities, namely harbor, shipbuilding, shipping, oil refineries and petrochemicals and, in addition, Genoa is also characterised by large metallurgical and steel plants.

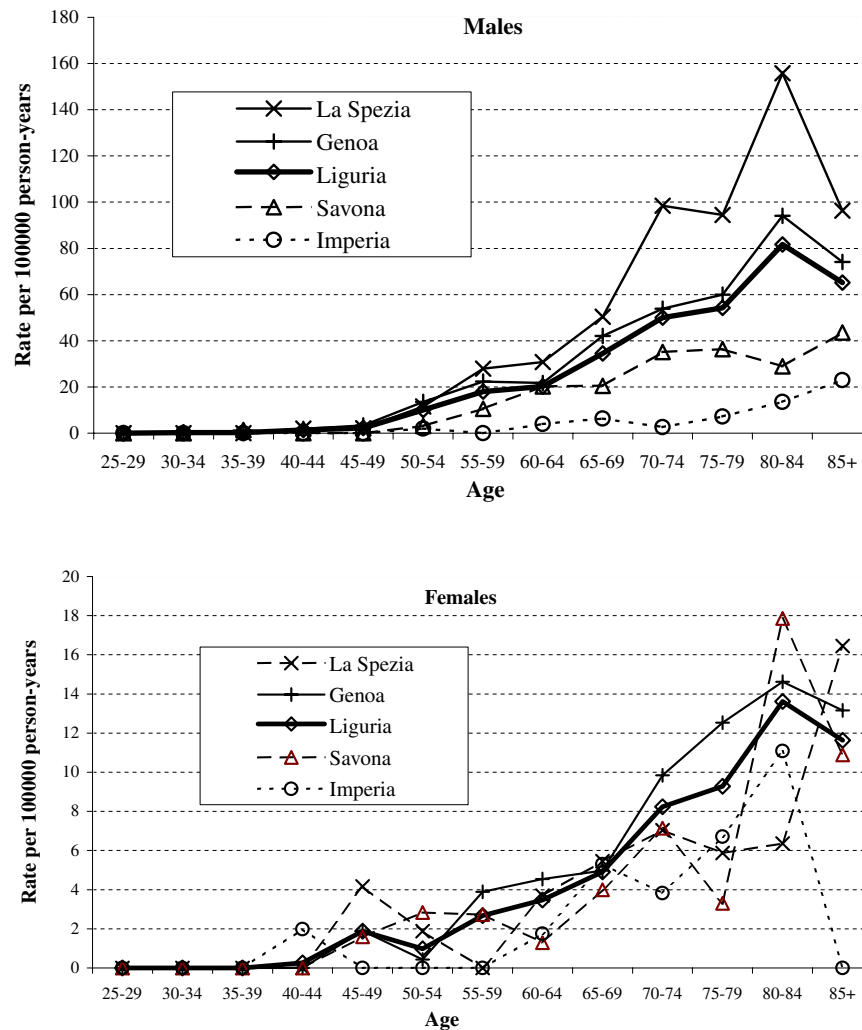


Fig. 2. Age specific incidence rate (per 100,000 person-years) for certified probable and possible pleural malignant mesothelioma by gender (1996–2002).

The large difference in incidence between males and females is another factor that strongly supports the definition of PMM as an occupational cancer associated with increased asbestos use that occurred about 20–50 years ago [17–19]. Despite this difference between sexes (m:f = 4:1), the number of females affected by PMM gave the impression of being extremely high, when 188 cases (19.9%) were observed during the covered seven years, particularly in the areas with higher incidence among men. This observation, together with the very high percentage of females with unknown asbestos exposure (53.4%), highlights the possible role of undetectable environmental exposure to asbestos.

Peculiarly, a similar males/females ratio of cases with unknown exposure to asbestos was observed among both sexes throughout the four provinces, strengthening the hypothesis that also environmental exposure to asbestos may occur in geographical areas where asbestos was heavily present in the work environments. This observation appears even more likely when we observe

that a $SRR = 2.12$ ($P < 0.05$, 95% CI 1.64–2.60) was estimated for females living in Genoa (where, as seen, the industrial concentration was really high) with respect to females living in the province of Imperia, which inversely showed contemporarily the lowest number of cases and the lowest number of occupationally exposed workers.

Some key factors such as long latency period, bad performance status of the patients, their (or next-of-kin's) and our ignorance on the materials used in the past and related risks may have affected, to some extent, our ability to detect past asbestos exposure. Nevertheless, the consistency of the number of patients with unknown asbestos exposure among both sexes and throughout the four provinces of Liguria is noteworthy and it is not, in our opinion, indication of poor quality but, on the contrary, a condition requiring more investigation. Anyway, according with some authors, 30–50% of the patients suffering from this disease were not employed in jobs well known for risk of asbestos exposure

Table 3
Distribution of pleural malignant mesothelioma incident cases by exposure information, gender and province

Exposure*	Imperia				Savona				Genoa				La Spezia				Total			
	Males		Females		Males		Females		Males		Females		Males		Females		Males		Females	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Certified professional	2	18.2	2	16.7	26	36.6	1	5	200	50.9	4	4.3	111	67.3	3	14.3	339	53	10	6.8
Probable professional	1	9.1	0	0	8	11.3	0	0	64	16.3	1	1.1	22	13.3	1	4.7	95	14.8	2	1.4
Possible professional	2	18.2	0	0	15	21.1	1	5	67	17	9	9.7	18	10.9	1	4.7	102	15.9	11	7.5
Household	0	0	0	0	0	0	2	10	2	0.5	20	21.5	0	0	6	28.7	2	0.3	28	19.2
Environmental	0	0	0	0	0	0	3	15	0	0	5	5.3	1	0.6	1	4.7	1	0.2	9	6.2
Hobbies	0	0	0	0	1	1.4	0	0	4	1	1	1.1	0	0	1	4.7	5	0.8	2	1.4
Unlikely	0	0	0	0	2	2.8	2	10	1	0.3	4	4.3	0	0	0	0	3	0.5	6	4.1
Unknown	6	54.5	10	83.3	19	26.8	11	55	55	14	49	52.7	13	7.9	8	38.2	93	14.5	78	53.4
Total	11	100	12	100	71	100	20	100	393	100	93	100	165	100	21	100	640	100	146	100
Ongoing definition	1	33.3	1	100	8	61.5	3	37.5	33	35.1	13	41.9	2	28.6	2	100	44	37.6	19	45.2
Unclassified (closed case)	2	66.7	0	0	5	38.5	5	62.5	61	64.9	18	58.1	5	71.4	0	0	73	62.4	23	54.8
Total	3	100	1	100	13	100	8	100	94	100	31	100	7	100	2	100	117	100	42	100
Total	14	–	13	–	84	–	28	–	487	–	124	–	172	–	23	–	757	–	188	–

Note: Certified professional: Individuals that have performed work tasks that implied the use or exposure to asbestos. Probable professional: Individuals that have worked in an industrial sector or working environment in which asbestos was certainly used or was present but for whom no exposure documents are available. Possible professional: Individuals that have worked in an industrial plant or in a working environment belonging to an economic sector in which the presence or use of asbestos had been revealed but no information available concerning individual's use or contact (if any) with asbestos. Household: Individuals not exposed professionally but exposed in the household due to cohabitation with at least one worker classed certified or probable professional. Environmental: Individuals not exposed professionally that lived close to processing facilities using asbestos or asbestos-containing products or that may have frequented for non professional reasons asbestos-containing premises. Non-professional: Individuals not exposed professionally that have been exposed as a result of activities performed in the household (use of asbestos household goods) or during leisure time (do-it-yourself, plumbing repairs, motor vehicle repairs, masonry work, etc.). Unlikely: Individuals for whom good quality data concerning professional and private history is available. Data allows to exclude asbestos exposure levels exceeding the "natural environment background level". Unknown: Individuals whose incomplete data set or for whom the current level of knowledge does not allow exposure class allocation. Ongoing definition: Individuals whose exposure assessment case is being defined through the acquisition of additional information. Unclassified: Individuals for whose cases no information is available nor will be available (closed case).

[8], suggesting that undetected asbestos exposure could have occurred in different areas.

The fact that not all cases of PMM show a clear association with asbestos exposure allows us to presume the presence of other possible causes, including possible interaction between undetected asbestos exposure and SV40 virus exposure [6,8,31,32] that could lead to an amplification of an otherwise negligible risk.

In conclusion, PMM incidence rates in Liguria remain high, especially in the provinces of La Spezia and Genoa, where many activities involving asbestos exposure, from shipyards, heavy or chemical industries, oil refineries and building activities existed. Moreover, the incidence rates are likely to increase due to the long average latency of PMM. The expected beneficial effects of Decree Law 257(1992) which banned asbestos use in Italy will probably only be observed much later on.

Conflict of interest statement

None declared.

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