Annals of Research in Oncology
Vol. 3(3), 109-118, 2023

RESEARCH ARTICLE

INCIDENCE AND ASBESTOS EXPOSURE OF MALIGNANT MESOTHELIOMA IN THE NORTH ITALIAN REGION

Lucia **Mangone** [1, 2, *], Isabella **Bisceglia** [1], Cinzia **Storchi** [1], Fortunato **Morabito** [3], Maria **Pagano** [4], Antonino **Neri** [5], Antonio **Romanelli** [2]

[1] Reggio Emilia Cancer Registry, Epidemiology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2] COR Emilia-Romagna, Epidemiology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3] Biotechnology Research Unit, AO di Cosenza, Aprigliano, Cosenza, Italy
[4] Medical Oncology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
[5] Scientific Directorate, Azienda Sanitaria Locale - IRCCS di Reggio Emilia, Italy
[*] Correspondence to: mangone.lucia@ausl.re.it, https://orcid.org/0000-0002-5089-5178.

ABSTRACT: This study aims to describe the incidence of malignant mesothelioma (MM) in the period 1996-2022 and report the related exposure to asbestos. The study includes all cases of MM with a certain or a probable diagnosis (with microscopic confirmation) and possible cases (without microscopic confirmation) collected by the Regional Mesothelioma Registry (ReM) which represents one of the 21 CORs (Regional Operational Centers) in Italy.
For each case, information on age, sex, tumor site, morphology, date of diagnosis, follow-up, and province of residence was collected. Data on previous occupational and non-occupational exposure to asbestos, by type of sector and activity, was also collected through an analytical questionnaire, administered to the patient or his closest relatives.
Between 1996 and 2022 were registered, 3,357 cases of MM classified as certain (2,870 cases, 85.5%), probable (174 cases, 5.2%), and possible cases (313 cases, 9.2%). The greatest number of cases were recorded for the pleura (3,081) and the peritoneum (245). The province of Bologna (741 cases), Reggio Emilia (508 cases), Parma (390 cases), and Modena (370 cases) recorded the highest number of cases, most of them were registered at age 75+ (1,575 cases).
Concerning exposure, 70.5% were defined as professional, 5.9% familiar, 2.2% as environmental, and 1.4% as extra professional. The majority of males had occupational exposure (83.3%) in comparison with 34.3% of women, who showed also family exposure in 20.3% of cases. Bologna confirms the primacy for professional and environmental exposure cases, Reggio Emilia for familiar, and Parma and Bologna for extra-professional exposure.

Doi: 0.48286/aro.2023.72

Impact statement: This paper provides 27 years of information on MM diagnosis and asbestos exposure, by age, sex, and province of residence.

Key words: *mesothelioma, incidence, exposure, asbestos.*

Received: July 28, 2023/**Accepted**: Aug 28, 2023/
Published: Sept 30, 2023

INTRODUCTION

Malignant mesothelioma (MM) represents the most frequent primary neoplasm of the mesothelium (1). It can originate from the pleura, peritoneum, pericardium, or tunica vaginalis of the testis. Exposure to asbestos, whether occupational, environmental, or familial, accounts for 90% of cases of mesothelioma, especially those with pleural origin (2-5). Due to its nature as an occupational disease, a national surveillance system is active with mandatory reporting; for this reason, the National Mesothelioma Register (ReNaM) exists in Italy and maintains records of all cases of MM and asbestos exposure (6). Although the use of asbestos has been banned in

Italy for nearly 30 years, there has not yet been a reduction in the incidence of mesothelioma in our country (7), due to the latency between exposure (8) to the mineral and the development of the disease. The most frequent histology is the epithelioid subtype accounting for 70-85% of cases, while the more aggressive sarcomatoid and biphasic forms are rarer (9). The WHO classification, in addition to diffuse mesothelioma, also identifies *localized* mesothelioma, a malignant neoplasm that appears as a single mass without clinical or histological evidence of diffusion on the serosa (10). The diagnostic gold standard is represented by pleural biopsies performed using video-assisted thoracoscopy (VATS) (11). However, a cytological examination of pleural fluid or percutaneous biopsy could be performed in selected cases (12).

Historically, age, sex, tumor grade and stage, and histology have been shown to be independent prognostic factors. Notably, worse prognosis has been reported for non-epithelioid histology *versus* the epithelioid subtype. The standard treatment is chemotherapy with a platinum derivative in combination with pemetrexed in epithelioid subtype (13). Recently, immunotherapy with the nivolumab ipilimumab combination has been approved in the first-line setting, although its use as a 'one size fits all' approach is highly debated (14-15).

Second-line treatment consists of gemcitabine or vinorelbine, rechallenged with pemetrexed-based regimens. A phase 2 study demonstrated increased survival from the addition of ramucirumab, a monoclonal antibody directed against the vascular endothelial growth factor receptor, to gemcitabine compared to second-line gemcitabine alone (16). Conversely, a Phase 3 study failed to demonstrate a progression-free interval (PFS) advantage of an immunotherapeutic approach with pembrolizumab (PD-1 inhibitor over standard chemotherapy in previously chemotherapy-exposed patients (17). Nevertheless, because of the rarity and serious prognosis of this disease, patient participation in clinical trials should be further encouraged (18).

Furthermore, the progressive elimination of asbestos from public and private environments represents a fundamental condition for achieving a continuing reduction in MM incidence (8). In Italy, asbestos was definitively banned in April 1994 (see Law 257/92); nevertheless, the long latency time between the exposure beginning and the onset of the disease, associated with the lengthening of life expectancy, and the improvement of diagnostic techniques, such as modern imaging techniques and advances in immunohistochemical staining, which have contributed to optimized MM diagnosis, have ultimately led to an increase in the incidence of MM in recent years (19, 20). The incidence of mesothelioma in several countries reflects historical patterns of commercial use of asbestos over the past century, and the predominant occupational exposures support the finding that mesothelioma is mostly diagnosed in males. MM remains a fatal cancer with a very poor prognosis, with a median survival of approximately 10 months from diagnosis (19, 21). Survival is highly variable, however, most people live for about a year after diagnosis. Efforts to improve and maintain the quality of life of mesothelioma patients remain a priority (22).

This study aims to report the incidence of MM in the period 1996-2022 with the related exposure to asbestos.

MATERIALS AND METHODS

The Regional ReM (Mesothelioma Registry), active since 01/01/1996, is a Cancer Registry (CR) specifically dedicated to the study of the incidence and etiology of MM. The ReM's objectives include identifying all cases of MM, gathering data for an accurate diagnostic definition, and standardizing the attribution of professional or extra-work asbestos exposure. The ReM additionally acts as the Emilia-Romagna COR (Regional Operational Centers) functions. In addition to the reports of the pathological investigations performed, medical records of significant hospitalizations carried out in public and private, regional, or extra-regional health institutes are collected.

The cases are collected from 1996 to 2022: however, the standardized rates and trends have been calculated up to 2021, because for 2022 the definitive link with the Cancer Registries is still missing. Incidence data are collected following the rules of population CRs (23) and coded by site and morphology according to ICDO-3 (24).

A trained group of professionals collects information on asbestos exposure by following an analytical questionnaire developed at the national level by National ReNaM (25). The detection network tends to acquire in real time the reports of new cases just diagnosed, for the early collection of the information on anamnestic exposure required di-

rectly from the patient. A panel of experts (which includes an occupational doctor, *etc*.) evaluates and discusses any exposure to asbestos and evaluates whether this is of a professional or environmental nature, *etc*.
Periodically (every 6 months) a link is made with the regional CRs to verify the completeness and accuracy of the information collected.

RESULTS

Between 1996 and 2022 in Emilia Romagna 3,357 MM were registered. Most of the cases (2,870 cases, equal to 85.5%) were classified as *certain*, 174 as *probable* (5.2%), and 313 (9.2%) as *possible* cases (**Table 1**). Eight cases were registered with the death certificate only (DCO) but they are not included in the incidence analyses. The exclusion of DCOs was implemented in this analysis as is usually done by Population Cancer Registries: analyses of incidence and survival never include DCOs (26).
Table 2 shows the distributions by site and year of diagnosis. Of the 3,357 tumors, 3,081 originated in the pleura, 245 in the peritoneum, 10 in the pericardium, and 21 in the testis. Until 2001 there were fewer than 100 cases per year. In 2011-2012 a peak was reached with over 150 cases and the trend maintained stable in recent years. The trend of cases is largely related to the growth in pleural tumors which have increased since the early 2000s and show no indication of decreasing.
As for age (**Table 3**), there is a strong gradient for pleural MM in both sexes. Most of the cases are recorded in ages 75+ (1,575), followed by 65-74 (1,069), 508 in ages 55-64, 157 cases in ages 45-54, and 48 cases were recorded in patients <45 years.
The distribution of cases and incidence rates, standardized (TSD - Tasso di Standardizzazione Diretto) on the Italian population, divided by males and females, are shown in **Figure 1**. Bologna (741), followed by Reggio Emilia (508), Parma (390) and Modena (370) are the provinces recording the highest number of cases. The highest standardized rates were accounted for in males registered in Reggio Emilia (5.6), Piacenza (5.1), and Ravenna (4.8); while in females, the highest rates are found in Reggio Emilia (2.2), followed by Parma (1.5). The incidence trend of all cases of MM by gender and year is shown in **Figure 2**. The trend shows a slight increase in the incidence in both males and females.
Of the 3,357 cases of MM, information on exposure to asbestos was collected in 2,887 cases, 206 were not defined and 264 were not classifiable (**Table 4**). 80% of patients were exposed to asbestos: 87% male and 62% female. Among males, 83.3% had occupational exposure and among women, 34.3% had occupational and 20.3% family exposure.
The distribution by exposure and province of residence is shown in **Table 5**. The largest number of patients with mesothelioma caused by occupational exposure is recorded in Bologna (442), followed by Reggio Emilia (341), Parma (247), and Ravenna (230).
Considering the working sector involved, most of the asbestos exposure is recorded in the construction sector and the railway sector (**Table 6**), mainly in males. Women, in general, are less affected, but most of the cases are recorded in the sectors of sugar refineries and the production of cement.

Table 1. *Distribution of cases by diagnostic definition.*

	N. CASES	DIAGNOSTIC DEFINITION
MM CERTAIN	2,870 (85%)	Histology presents with characteristic morphological picture; characteristic/ suggestive/absent immuno-histochemistry + diagnostic confirmation by imaging/ clinical diagnosis of discharge
MM PROBABLE	174 (5%)	Histology presents with dubious morphological picture or cytology with characteristic picture + diagnostic confirmation by imaging/clinical diagnosis of discharge
MM POSSIBLE	313 (10%)	Absent histology/cytology, indicative clinical and radiological data + diagnosis of MM CC discharge
TOTAL	3,357	

Table 2. *Distribution of cases by site and year of diagnosis.*

YEAR	SITE				TOTAL
	Pleura	Peritoneum	Pericardium	Testis	
1996	63	8	-	2	73
1997	70	7	3	-	80
1998	77	4	1	1	83
1999	67	6	-	-	73
2000	76	9	-	1	86
2001	88	6	-	2	96
2002	98	15	-	1	114
2003	97	6	1	1	105
2004	110	8	2	-	120
2005	107	10	-	2	119
2006	100	7	-	-	107
2007	101	14	-	-	115
2008	122	9	-	1	132
2009	111	11	-	-	122
2010	117	12	1	-	130
2011	144	10	-	1	155
2012	142	10	1	2	155
2013	146	5	-	1	153
2014	121	11	-	1	133
2015	141	10	-	-	151
2016	150	10	-	-	160
2017	146	10	-	1	157
2018	143	14	-	-	157
2019	138	8	-	-	146
2020	135	7	1	1	144
2021	148	9	-	1	158
2022	123	9	-	2	134
Total	3,081 92%	245 7%	10 0.3%	21 0.7%	3,357

Table 3. *Distribution of cases by sex, site, and age at diagnosis.*

AGE	MALE				FEMALE			TOTAL
	Pleura	Peritoneum	Pericardium	Testis	Pleura	Peritoneum	Pericardium	
<45	19	9	-	4	11	5	-	48
45-54	94	10	-	5	38	9	1	157
55-64	348	26	-	3	104	25	2	508
65-74	744	46	4	4	240	30	1	1,069
75+	1,056	48	1	5	427	37	1	1,575
Total	2,261	139	5	21	820	106	5	3,357

Table 4. *Distribution of malignant mesothelioma by type of exposure and sex.*

TYPE OF EXPOSURE	MALE		FEMALE		TOTAL	
	N. cases	%	N. cases	%	N. cases	%
Professional	1,774	83.3	260	34.3	2,034	70.5
Familiar	17	0.8	154	20.3	171	5.9
Environmental	31	1.4	33	4.4	64	2.2
Extra Professional	20	1.0	19	2.5	40	1.4
Improbable	63	3.0	87	11.5	150	5.2
Unknown	223	10.5	205	27.0	428	14.8
Total of defined cases	2,129	100.0	758	100.0	2,887	100.0
To be defined	140	5.8	66	7.1	206	6.1
Not classifiable	157	6.5	107	11.5	264	7.9
Total of incident cases	2,246		931		3,357	

Table 5. *Distribution of cases by type of exposure and province of residence.*

TYPE OF EXPOSURE	N. CASES									
	Piacenza	Parma	Reggio Emilia	Modena	Bologna	Ferrara	Ravenna	Forlì-Cesena	Rimini	Emilia-Romagna E-R
Professional	162	247	341	184	442	192	230	147	89	2,034
Familiar	14	21	40	10	39	20	8	9	10	171
Environmental	3	14	9	6	21	3	3	4	1	64
Extra-professional	5	8	1	4	8	2	6	4	2	40
Improbable	12	20	8	15	41	14	24	8	8	150
Unknown	46	52	28	44	121	36	43	36	22	428
To be defined	4	9	72	45	27	17	26	1	4	206
Not classifiable	35	19	9	62	42	44	6	27	20	264
Total	282	390	508	370	741	328	346	236	156	3,357

DISCUSSION

This work aims to report the incidence data and asbestos exposure of MM in a region of North Italy. The data are collected from a specialized Cancer Registry and, among the first objectives of a CR, are the accuracy and completeness of the cases (27). These two objectives seem to be achieved in this work since 91% of the cases have a microscopic confirmation, often supported by immunohistochemistry, and because the involvement of a regional network and the link with population CRs ensures the non-loss of cases.

The study reports 3,357 cases of MM registered in Emilia-Romagna from 1996 to 2022. In 26 years of registration, 3,357 cases of MM were collected, mainly involving pleura (92%). Few cases were detected in the peritoneum (7%), and very few in testis (0.7%), and pericardium (0.3%). Our incidence overlaps that reported in the literature even if the high number of cases of the extra-pleura cases seems more linked to a specific ability of the CR to intercept these neoplasms than to a higher incidence (28-30). Over the years there has been an increase in diagnoses, especially involving the pleura, which reached 100 cases per year in the early 2000s and 150 cases

Table 6. *Distribution of occupational exposure to asbestos by the main sector of economic activity and sex.*

PRODUCTION SECTOR	MALE		FEMALE		TOTAL	
	N. cases	%	N. cases	%	N. cases	%
Constructions	282	15.9	1	0.4	283	13.9
Constructions/Repair Railway Rolling Stocks	204	11.5	3	1.2	207	10.2
Engineering industry	167	9.4	14	5.4	181	8.9
Sugar Refineries/Other Food Industries	121	6.8	43	16.6	164	8.1
Production of Cement/Asbestos Products	98	5.5	33	12.7	131	6.5
Production of Chemical/Plastic Material	107	6.0	6	2.3	113	5.6
Building Completion Works	94	5.3	2	0.8	96	4.7
Glass / Ceramic/Rubber Manufacturing	64	3.6	24	9.2	88	4.3
Transportation	84	4.7	4	1.5	88	4.3
Production/Repair Vehicles (no trains and ships)	76	4.3	6	2.3	82	4.0
Manufacturing/Processing of Metallic Products	63	3.6	5	1.9	68	3.3
Textile industry	39	2.2	17	6.5	56	2.8
Trade	45	2.5	10	3.8	55	2.7
Production Electricity, Gas, Water	48	2.7	-	-	48	2.4
Social Services/Recreational Activities/ Healthcare	22	1.2	21	8.1	43	2.1
National Defense	38	2.2	1	0.4	39	1.9
Agriculture/Animal breeding	26	1.5	13	5.0	39	1.9
Metallurgical Industry	33	1.9	4	1.5	37	1.8
Other Manufacturing Industries	30	1.7	3	1.2	33	1.6
Other	133	7.5	50	19.2	183	9.0
Total	1,774	100.0	260	100.0	2,034	100.0

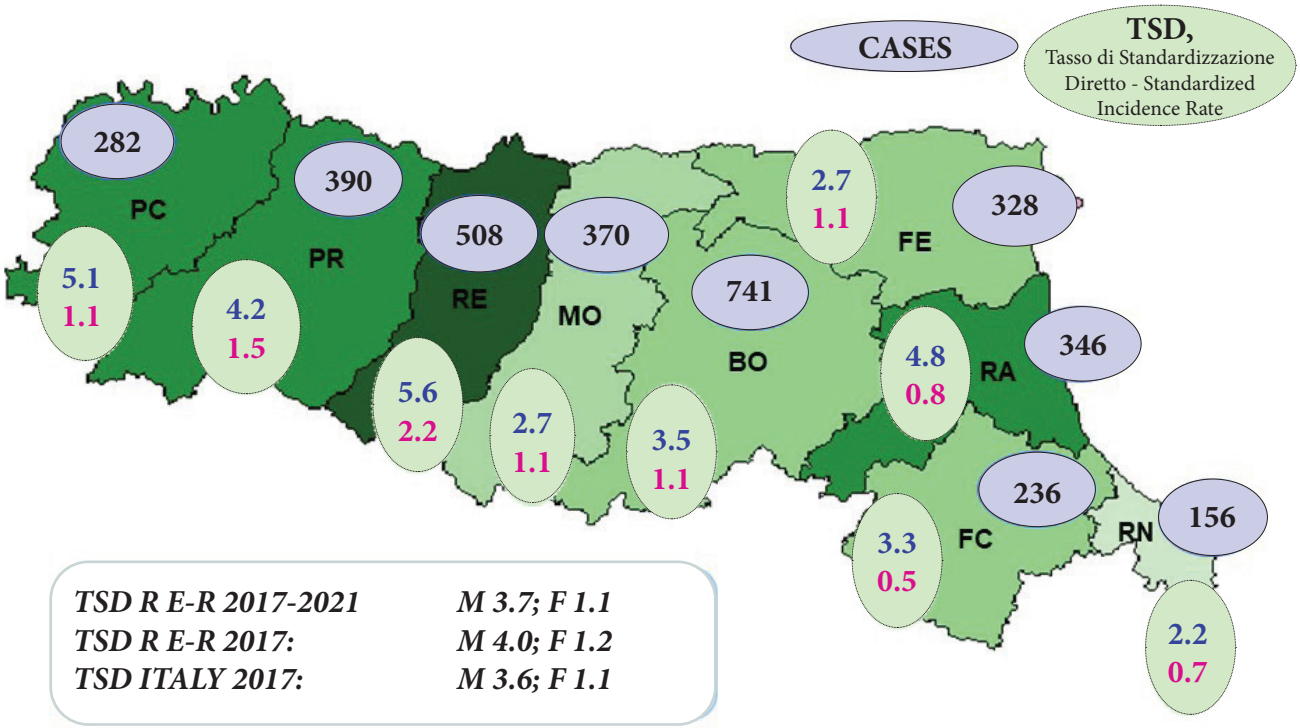

Figure 1. *ReM cases 1996-2022. Distribution of cases and standardized rates by province of residence (TSD).*

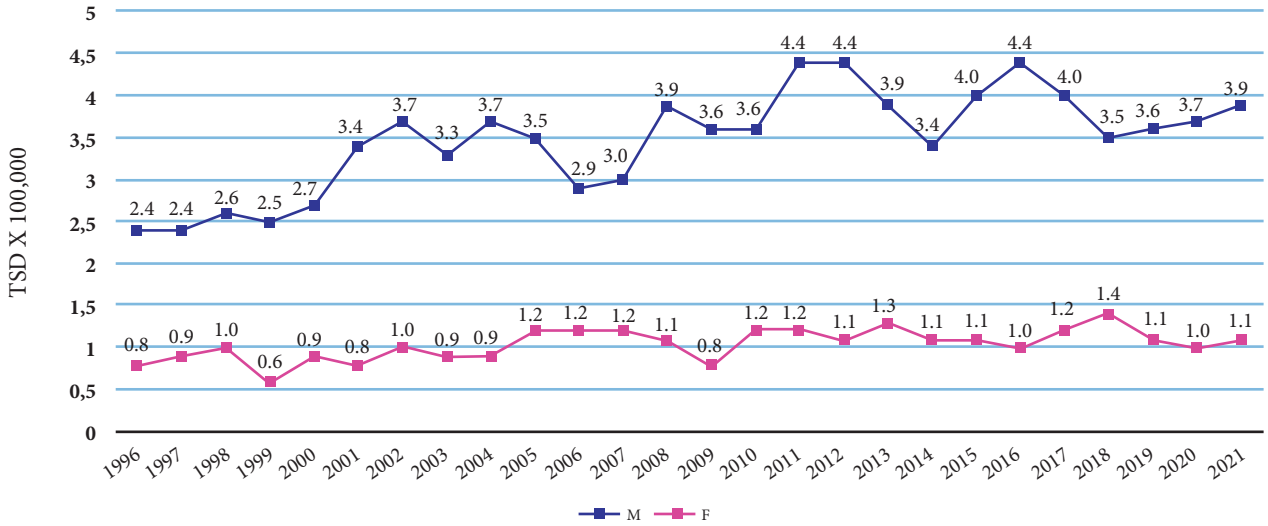

Figure 2. *Standardized incidence rates on the Italian population x 100,000 by year and sex. Year 1996-2021.*

since 2010 and the trend does not seem to be decreasing. Because all suspended and suspect diagnoses will be validated in the next months, the 134 MM observed in 2022 should not be interpreted as a definitive decrease in incidence. On the other hand, as previously documented (31), a late influence of Covid-19 on a decline in new diagnoses delayed compared to the initial waves cannot be disregarded. The trend is also confirmed by the standardized incidence rate which had doubled in our region going from 2.4 x 100,000 in 1996 to 3.9 in 2021 in males, while in females the trend was more constant.

In the literature, the MM trend shows variable rates with a decrease in some countries and stability or an increase in others, always linked to the various actions to remove the use of asbestos in production activities (8, 32, 33).

MM is a typical tumor of the elderly (46.9% of tumors resulted in age 75+ and 31.9% between 65-74 years), but cases diagnosed at a younger age are not uncommon (48 cases <45 years and 147 cases between 45-54 years). It should be noted that pleural mesothelioma at a young age has an M/F ratio of 1.7 while in later ages it is equal to 3:1, while for peritoneal tumors the ratio is almost always 1:3. The presence of cases of MM before the age of 45 is surprising given that in recent years more and more evidence documents a latency between exposure and onset of the disease around the age of 40 (34, 35). The distribution of cases by province is very interesting in our region, reflecting well the employment of workers in some production sectors and the employment of women in some companies existing in the area. The standardized rate in Emilia-Romagna in 2017 was 4.0 in males and 1.2 in females, slightly higher than the standardized rate recorded in Italy (36). In our study, the highest rate was recorded in Reggio Emilia in both males and females (5.6 and 2.2, respectively), followed by Piacenza (5.1) and Ravenna (4.8) in males and Parma in females (1.5). This high rate is in line with the presence in the province of Reggio Emilia of a high percentage of females working in the production of asbestos-cement products in the post-war period (37).

As far as exposure is concerned, it should be noted that the questionnaire was completed in 2,887 cases (86%) and, in most cases, directly from the patient's hands-free voice. To thoroughly collect exposure data, "real-time" enrolment is preferable (38). Asbestos exposure was confirmed in 80% of cases (86.6% in males and 61.4% in females). Among men, occupational exposure was recorded (83.3% of cases), while familiar, environmental, and extra-work exposures are very low (**Table 4**). In women, on the other hand, 34% of cases have professional exposure, 27.2% non-professional, 11.5% improbable and unfortunately 27% have unknown exposure in which, despite the available documentation, it has not been possible to identify with certainty a possible expository source. Occupational asbestos exposure is most often reported in men working in industries such as construction and manufacturing. In the United States, the age-adjusted death rate per 1 million women declined significantly, from 4.83 in 1999 to 4.15 in 2020: the larg-

est number of deaths was associated with the health care and social assistance industry (15.7%) and homemaker occupation (22.8%) (39). Asbestos exposure is mentioned in only a few of the studies that include women. We estimate that the risk of MM among females is close to that of males. The absence of detailed exposure histories should be rectified in future studies involving women (40). In the Emilia-Romagna Region, the production sectors most involved in the onset of MM were building constructions (subjects distributed evenly throughout the region) in 13.9% of cases, construction/repair of railway rolling stock (cases mostly resident in the provinces of Bologna and Reggio Emilia) in 10.2%, metalworking industry (8.9%), sugar refineries/other food industries (8.1%), and production of asbestos cement products (6.5%).

CONCLUSIONS

The study systematically collects MM data recorded in a region of northern Italy. The high percentage of microscopic confirmations and the large number of questionnaires administered to patients allowed to collect detailed information in a high percentage of cases. Unfortunately, the lack of data such as stage of the disease, diagnostic procedures, treatment, and, above all, quality of life of patients, represent a limitation to population-based registration. MM remains a low-incidence but high-mortality disease. It is necessary to keep the attention of health professionals, citizens, and the scientific community high on this disease to ensure patients the best treatment options and, on the other hand, the recognition of an indemnity when occupational exposure is recognized.

ACKNOWLEDGMENTS

The collection, archiving, and definition of malignant MM cases incidents throughout the Emilia-Romagna Region as possible, with an acceptable cost/benefit ratio, only through the effective collaboration and careful development of the regional detection network which has over 140 formally designated Referents, including pathologist specialists, hygienists and occupational doctors from the Departments of Public Health, pulmonologists, general surgeons, gynecologists urologists, oncologists, but also internists and cardiologists that the good collaboration established can guarantee an increasingly adequate knowledge of this fearful pathology.

COMPLIANCE WITH ETHICAL STANDARDS

Fundings

This study was partially supported by the Italian Ministry of Health - Ricerca Corrente Annual Program 2024.

Conflict of interests

The Authors have declared no conflict of interests.

Authors' contributions

LM: conceptualization, investigation, writing-original draft, visualization, supervision; IB: writing, review and editing, supervision; CS: investigation, supervision. FM: visualization, supervision; MP: visualization, supervision; AN: supervision; AR: conceptualization, investigation, writing original draft, visualization, supervision. All Authors have read and agreed to the published version of the manuscript.

Availability of data and materials

All the data supporting the findings of this study are available within the article and can be shared just before a reasonable request to the corresponding author.

Ethical approval

N/A.

Publication ethics

Plagiarism

The contents of the article are original and any overlaps with other articles are by the Authors themselves and appropriately cited.

Data falsification and fabrication

All the data correspond to the real.

REFERENCES

1. Hajj GNM, Cavarson CH, Pinto CAL, Venturi G, Navarro JR, Lima VCC. Malignant pleural mesothelioma: an update. J Bras Pneumol. 2021;47(6):e20210129. doi: 10.36416/1806-3756/e20210129.
2. Marinaccio A, Binazzi A, Marzio DD, Scarselli A, Verardo M, Mirabelli D, et al. Pleural malignant mesothelioma epidemic: incidence, modalities of asbestos exposure and occupations involved from the Italian National Register. Int J Cancer.

2012;130(9):2146-54. doi: 10.1002/ijc.26229.
3. Delgermaa V, Takahashi K, Park EK, Le GV, Hara T, Sorahan T. Global mesothelioma deaths reported to the World Health Organization between 1994 and 2008. Bull World Health Organ. 2011;89(10):716-24, 724A-724C. doi: 10.2471/BLT.11.086678.
4. Bertazzi PA. Descriptive epidemiology of malignant mesothelioma. Med Lav. 2005;7(4):287-303. PMID: 16457426.
5. Magnani C, Bianchi C, Chellini E, Consonni D, Fubini B, Gennaro V, et al. III Consensus Conference on Malignant Mesothelioma of the Pleura. Epidemiology, Public Health and Occupational Medicine related issues. Med Lav. 2015;106(5):325-32. PMID: 26384258.
6. Airoldi C, Ferrante D, Miligi L, Piro S, Stoppa G, Migliore E, et al. Estimation of Occupational Exposure to Asbestos in Italy by the Linkage of Mesothelioma Registry (ReNaM) and National Insurance Archives. Methodology and Results. Int J Environ Res Public Health. 2020;17(3):1020. doi: 10.3390/ijerph17031020.
7. Oddone E, Bollon J, Nava CR, Bugani M, Consonni D, Marinaccio A, et al. Predictions of Mortality from Pleural Mesothelioma in Italy After the Ban of Asbestos Use. Int J Environ Res Public Health. 2020;17(2):607. doi: 10.3390/ijerph17020607.
8. Alpert N, van Gerwen M, Taioli E. Epidemiology of mesothelioma in the 21st century in Europe and the United States, 40 years after restricted/banned asbestos use. Transl Lung Cancer Res. 2020;9(Suppl 1): S28-S38. doi: 10.21037/tlcr.2019.11.11.
9. Escalon JG, Harrington KA, Plodkowski AJ, Zheng J, Capanu M, Zauderer MG, et al. Malignant Pleural Mesothelioma: Are There Imaging Characteristics Associated With Different Histologic Subtypes on Computed Tomography? J Comput Assist Tomogr. 2018;42(4):601-6. doi: 10.1097/RCT.0000000000000727.
10. Marchevsky AM, Khoor A, Walts AE, Nicholson AG, Zhang YZ, Roggli V, et al. Localized malignant mesothelioma, an unusual and poorly characterized neoplasm of serosal origin: best current evidence from the literature and the International Mesothelioma Panel. Mod Pathol. 2020;33(2):281-96. doi: 10.1038/s41379-019-0352-3.
11. Migliore M, Fiore M, Filippini T, Tumino R, Sabbioni M, Spatola C, et al. Comparison of video-assisted pleurectomy/decortication surgery plus hyperthermic intrathoracic chemotherapy with VATS talc pleurodesis for the treatment of malignant pleural mesothelioma: A pilot study. Heliyon. 2023;9(6):e16685. doi: 10.1016/j.heliyon.2023.e16685.
12. Pairman L, Beckert LEL, Dagger M, Maze MJ. Evaluation of pleural fluid cytology for the diagnosis of malignant pleural effusion: a retrospective cohort study. Intern Med J. 2022;52(7):1154-9. doi: 10.1111/imj.15725.
13. Miyamoto Y, Kozuki T, Aoe K, Wada S, Harada D, Yoshida M, et al. JME-001 phase II trial of first-line combination chemotherapy with cisplatin, pemetrexed, and nivolumab for unresectable malignant pleural mesothelioma. J Immunother Cancer. 2021;9(10):e003288. doi: 10.1136/jitc-2021-003288.
14. Available from: https://www.nice.org.uk/guidance/ta818/documents/html-content-4. Accessed: Aug 29, 2023.
15. Meirson T, Pentimalli F, Cerza F, Baglio G, Gray SG, Correale P, et al. Comparison of 3 Randomized Clinical Trials of Frontline Therapies for Malignant Pleural Mesothelioma. JAMA Netw Open. 2022;5(3):e221490. doi: 10.1001/jamanetworkopen.2022.1490.
16. Pinto C, Zucali PA, Pagano M, Grosso F, Pasello G, Garassino MC, et al. Gemcitabine with or without ramucirumab as second-line treatment for malignant pleural mesothelioma (RAMES): a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Oncol. 2021;22(10):1438-47. doi: 10.1016/S1470-2045(21)00404-6.
17. Paz-Ares L, Vicente D, Tafreshi A, Robinson A, Soto Parra H, Mazières J, et al. A Randomized, Placebo-Controlled Trial of Pembrolizumab Plus Chemotherapy in Patients With Metastatic Squamous NSCLC: Protocol-Specified Final Analysis of KEYNOTE-407. J Thorac Oncol. 2020;15(10):1657-69. doi: 10.1016/j.jtho.2020.06.015.
18. Johnson M, Allmark P, Tod A. Living beyond expectations: a qualitative study into the experience of long-term survivors with pleural mesothelioma and their carers. BMJ Open Respir Res. 2022;9(1):e001252. doi: 10.1136/bmjresp-2022-001252.
19. Magnani C, Fubini B, Mirabelli D, Bertazzi PA, Bianchi C, Chellini E, et al. Pleural mesothelioma: epidemiological and public health issues. Report from the Second Italian Consensus Conference on Pleural Mesothelioma. Med Lav. 2013;104(3):191-202. PMID: 23879063.
20. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Arsenic, metals, fibres, and dusts. IARC Monogr Eval Carcinog Risks Hum. 2012;100(Pt C):11-465. PMID: 23189751.

21. Alessi M, Amadori D, Amunni G, Ascoli V, Barbina P, Bergamaschi A, et al. Stato dell'arte e prospettive in materia di contrasto alle patologie asbesto-correlate; Quaderni del Ministero della Salute, n° 15, maggio-giugno 2012. Available from: https://www.salute.gov.it/imgs/C_17_pubblicazioni_2570_allegato.pdf. Accessed: Aug 29, 2023.
22. Brims F. Epidemiology and Clinical Aspects of Malignant Pleural Mesothelioma. Cancers. 2021;13(16):4194. doi: 10.3390/cancers13164194.
23. Associazione Italiana Registri Tumori e AIRTUM Working Group. Manuale di tecniche di registrazione dei tumori. Casa Editrice Piccin, Padova, Sept 2021.
24. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al. International Classification of Disease for Oncology. 3rd Edition. World Health Organization, printed in Malta, 2013. Available from: 9789241548496_eng.pdf;sequence=1 (who.int). Accessed: Aug 29, 2023.
25. Nesti M, Adamoli S, Ammirabile F, Istituto Superiore di Sanità. Linee Guida per la rilevazione e la definizione dei casi di mesotelioma maligno e la trasmissione delle informazioni all'ISPESL da parte dei Centri Operativi Regionali. 2nd Edition, Roma, May 2004.
26. Parkin DM, Hakulinen T. Cancer registration: principles and methods. Analysis of survival. IARC Sci Publ. 1991;(95):159-76. PMID: 1894319.
27. Zanetti R, Schmidtmann I, Sacchetto L, Binder-Foucard F, Bordoni A, Coza D, et al. Completeness and timeliness: Cancer registries could/should improve their performance. Eur J Cancer. 2015;51(9):1091-8. doi: 10.1016/j.ejca.2013.11.040.
28. Mangone L, Romanelli A, Campari C, Candela S. Il mesotelioma maligno in Emilia-Romagna: incidenza ed esposizione ad amianto. Epidemiol Prev. 2002;26(3): 124-9. PMID: 12197049.
29. Peto J, Decarli A, La Vecchia C, Levi F, Negri E. The European mesothelioma epidemic. Br J Cancer. 1999;79(3-4):666-72. doi: 10.1038/sj.bjc.6690105.
30. Spirtas R, Heineman EF, Bernstein L, Beebe GW, Keehn RJ, Stark A, et al. Malignant mesothelioma: attributable risk of asbestos exposure. Occup Environ Med. 1994;51(12):804-11. doi: 10.1136/oem.51.12.804.
31. Mangone L, Mancuso P, Bisceglia I, Giorgi Rossi P, Chellini E, Negro C, et al; ReNaM Working Group. The impact of COVID-19 on new mesothelioma diagnoses in Italy. Thorac Cancer. 2022;13(5):702-7. doi: 10.1111/1759-7714.14296.
32. Nuyts V, Nawrot T, Nemery B, Nackaerts K. Hotspots of malignant pleural mesothelioma in Western Europe. Transl Lung Cancer Res. 2018;7(5):516-9. doi: 10.21037/tlcr.2018.10.01.
33. Zhai Z, Ruan J, Zheng Y, Xiang D, Li N, Hu J, et al. Assessment of Global Trends in the Diagnosis of Mesothelioma From 1990 to 2017. JAMA Netw Open. 2021;4(8):e2120360. doi: 10.1001/jamanetworkopen.2021.20360.
34. Carbone M, Adusumilli PS, Alexander HR Jr, Baas P, Bardelli F, Bononi A, et al. Mesothelioma: Scientific clues for prevention, diagnosis, and therapy. CA Cancer J Clin. 2019;69(5):402-29. doi: 10.3322/caac.21572.
35. Huh DA, Chae WR, Choi YH, Kang MS, Lee YJ, Moon KW. Disease LatencyAccordingg to Asbestos Exposure Characteristics among Malignant Mesothelioma and Asbestos-Related Lung Cancer Cases in South Korea. Int J Environ Res Public Health. 2022;19(23):15934. doi: 10.3390/ijerph192315934.
36. Fazzo L, Minelli G, De Santis M, Ceccarelli E, Iavarone I, Zona A. The Epidemiological Surveillance of Mesothelioma Mortality in Italy as a Tool for the Prevention of Asbestos Exposure. Int J Environ Res Public Health. 2023;20(11):5957. doi: 10.3390/ijerph20115957.
37. Bracke M, Clifford R, Donert C, Glynn R, McLellan J, Todd S. Women, Work and Value in Post-War Europe: Introduction. Contemporary European History. 2019;28(4):449-53. doi: 10.1017/S0960777319000225.
38. van Gerwen M, Alpert N, Flores R, Taioli E. An overview of existing mesothelioma registries worldwide, and the need for a US Registry. Am J Ind Med. 2020;63(2):115-20. doi: 10.1002/ajim.23069.
39. Mazurek JM, Blackley DJ, Weissman DN. Malignant Mesothelioma Mortality in Women - United States, 1999-2020. MMWR Morb Mortal Wkly Rep. 2022;71(19):645-9. doi: 10.15585/mmwr.mm7119a1.
40. Baur X, Frank AL, Soskolne CL, Oliver LC, Magnani C. Malignant mesothelioma: Ongoing controversies about its aetiology in females. Am J Ind Med. 2021;64(7):543-50. doi: 10.1002/ajim.23257.