

Epidemiology of Malignant Pleural Mesotheliomas in Croatia in the Period from 1989 to 1998

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ABSTRACT

Malignant pleural mesotheliomas are rare tumors. Their occurrence is often associated with the exposure to asbestos. Asbestos is widely used in various industries as well as for many types of products in everyday use. In Croatia in the period from 1989 to 1998, the rate of incidence was 0.4–1.1 / 100,000. The highest rate of incidence was in the Districts of Istria (2.9) and Split-Dalmatia (2.5). It is more frequent among males than among females with a ratio of 3.2:1. It rarely occurs before the age of 40 and most of the patients suffering from the disease are more than 65 years old. About 12% of mesotheliomas metastasize into regional lymph nodes and 17% of them into distant organs. The disease unavoidably leads to death and, according to the data obtained in Croatia in the period from 1989 to 1998 the mortality and incidence are very close.

Introduction

Mesotheliomas are tumors that derive from mesothelial cells. Beside pleura, the primary manifestation can occur in pericardium, peritoneum and layers of testes. The ratio between pleural mesotheliomas and other localizations is 10:1. Malignant pleural mesotheliomas can be divided into localized and diffuse. Localized mesotheliomas can be benignant or malignant whereas the diffuse are always malignant.

The exposure to asbestos has been referred to in the studies of etiology of pleural mesotheliomas for a long time. Zeolite is also occasionally referred too¹. Many reports and results of research dealing with workers, who were in contact with asbestos, have demonstrated the etiological connection between the exposure to asbestos and the occurrence of malignant pleural mesotheliomas^{2–5}.

In nature asbestos can be found in the form of silicate and it comes in about thirty varieties. Most widely used types of asbestos are chrysotile, crocidolite, anthophyllite and amosite. It is used in shipyards as well as in construction and automotive industries. More than 3,000 various industrial products contain asbestos⁶.

Most frequently asbestos dust is inhaled but it can also occur when water and soil near asbestos mines and processing plants which use asbestos, are polluted. In addition, asbestos can be a hazard to the families of asbestos workers, who may carry asbestos dust home on their clothing or even in their hair. There is also a high risk of exposure to asbestos that is not occupationally related because a great number of products in everyday use contain asbestos. According to some authors, 30–50% of the patients suffering from the disease do not hold such jobs in which they are exposed to asbestos⁶.

Many studies report on oncogenic effects of short-fiber type of asbestos, e.g. crocidolite, whereas long-fiber chrysotile has fibrinogenic effects. The exposure to asbestos that results in oncogenic effects has to be long-term, from 10 to 20 years. In addition to length, the intensity of exposure is also important. From the time of exposure to asbestos dust to the manifestation of the disease there is a long-lasting latent period of 20–40 years, which is explained by the slow elimination of asbestos from the lungs⁶.

Patients and Methods

The data published in the bulletins of the Croatian Institute for Public Health, Department of Epidemiology, in the period from 1989 to 1998, were analyzed retrospectively. The data were collected and published by the Register for Cancer of the Republic of Croatia that used hospital Patient Statistical Forms (type »on-

co») and the Reports on Malignant Neoplasm from outpatient departments and doctor's offices. The copies of histological and cytological findings were also used. The number of new cases of mesotheliomas in relation to sex and age, the rate of incidence on 100,000 of population in relation to sex and age as well as the number and percentage of new cases of mesotheliomas according to the stage of the disease were all shown. The data on the number of deaths were collected at the State Statistical Institute.

Results

Three hundred and forty three patients suffering from malignant pleural mesothelioma were registered in Croatia in the period from 1989 to 1998. Among these 343 patients there were 262 males and 81 females. On average there were 35 patients suffering from pleural mesothelioma registered per year and about thirty patients died in the course of one year.

The smallest number of patients was registered in 1991 (n=19) but that was the first year of the Croatian War of Independence in which the reports on the number of patients were not sent from the occupied areas. The largest number of the patients affected with the disease was recorded in 1995 (n=46) and 1996 (n= 50), exactly when the new International Classification of the Diseases started being used. This leads us to believe that some other disease of the pleura might have been registered under the code of mesothelioma (Table 1).

The rate of incidence in Croatia in the period from 1989 to 1998 was 0.4–1.1/100,000, the mean rate being 0.7/100,000. In males it was 1.1, and in females it was 0.3 on 100,000 (Figure 1). According to the data collected by the Register for Cancer, in 1998 the highest rate of incidence was in the County of Istria (2.9 /

TABLE 1
INCIDENCE RATE AND MORTALITY FROM MALIGNANT PLEURAL MESOTHELIOMA
IN CROATIA FROM 1989 TO 1998

Year	Incidence			Mortality		
	Males (N=262)	Females (N=81)	Total (N=343)	Males (N=223)	Females (N=63)	Total (N=286)
1989	16	8	24	15	7	23
1990	24	7	31	24	5	29
1991	16	3	19	14	2	16
1992	21	6	27	19	5	24
1993	26	11	37	20	10	30
1994	25	9	34	23	5	28
1995	29	17	46	27	12	39
1996	42	8	50	36	7	43
1997	36	6	42	34	4	38
1998	27	6	33	22	6	28

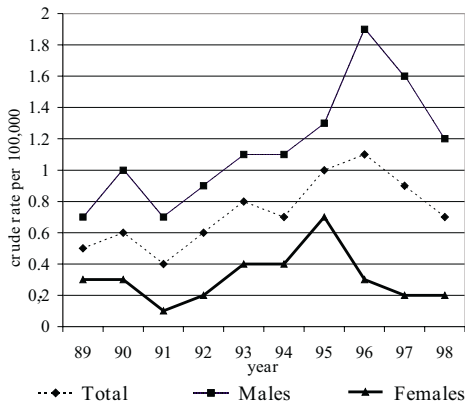


Fig. 1. Incidence rate of malignant pleural mesothelioma in Croatia from 1989 to 1998.

Fig. 2. Incidence rate of malignant pleural mesothelioma by Counties during the year 1998.

100,000) and Split and Dalmatia (2.5 / 100,000). These are the Counties with a developed shipbuilding industry. Not a single case of mesothelioma was recorded in 1998 in the mainly agricultural counties such as the

County of Lika and Senj, the County of Virovitica and Podravina and the County of Krapina and Zagorje (Figure 2).

Malignant pleural mesotheliomas appear occasionally before the age of 35. In Croatia in the period from 1989 to 1998 there was one patient recorded in the age group 25–29 and one patient in the age group 30–34, there were five patients in the age group 35–39 and twenty in the age group 40–44. The greatest number (n=120) was registered with the patients

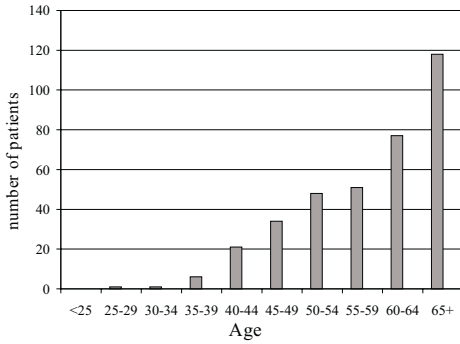


Fig. 3. Incidence of malignant pleural mesothelioma by age from 1989 to 1998.

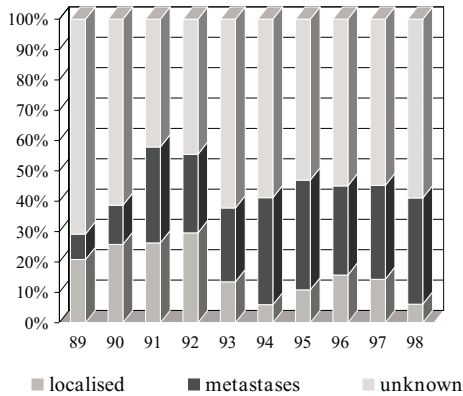


Fig. 4. Percentage of new cases of malignant pleural mesothelioma by stage from 1989 to 1998.

who were more than 65 years old (Figure 3). Malignant pleural mesotheliomas in 30–50% of cases metastasize either into regional lymph nodes or into distant organs. According to the Register for Cancer of the Republic of Croatia, in the period from 1989 to 1998 in 55.2% of the newly registered patients the stage of disease was not indicated, 15.8% had the disease at a localized stage, 12% had metastases into regional lymph nodes and 17% of them had metastases into distant organs⁷ (Figure 4).

Malignant pleural mesotheliomas rate as the most malignant tumors. The dis-

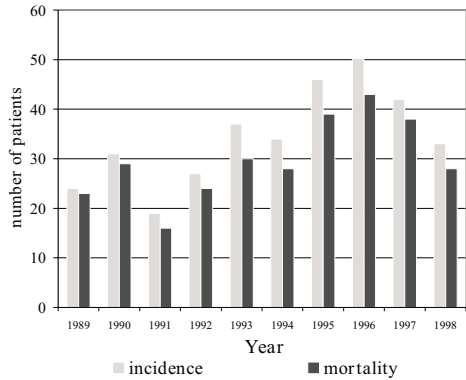


Fig. 5. Incidence and mortality of malignant pleural mesothelioma in Croatia from 1989 to 1998.

ease unavoidably leads to a fatal outcome. In Croatia in the period from 1989 to 1998 the incidence and mortality are very close which can be seen in the Figure 5.

Discussion

Malignant pleural mesotheliomas are rare tumors. They are very aggressive and their incidence is increasing every year. According to the experts' opinion this increase will continue until 2030⁸.

The incidence of malignant pleural mesotheliomas in the world is 0.1–1.5 / 100,000 and with the exposed ones it is 6–11 / 100⁹. In the countries of Western Europe the rate of incidence in males is approximately the same as in Croatia whereas in the countries of Eastern Europe it is significantly lower. The incidence in females is approximately the same in all the stated countries¹⁰ (Table 2).

The incidence of pleural mesotheliomas increases with age. According to the data in literature it rarely occurs before the age of 40 and the greatest number of the patients who suffer from it are over 65. It is exactly the same in Croatia where the greatest number of patients suffering from mesothelioma is over 65 (n=

TABLE 2
INCIDENCE RATE OF MALIGNANT PLEURAL
MESOTHELIOMA IN SOME EUROPEAN
COUNTRIES IN THE YEAR 2000

Country	Incidence rate per 100,000		
	Males	Females	Total
Croatia	1.1	0.3	0.7
Denmark	1.4	0.3	0.9
Germany	0.9	0.3	0.6
Austria	0.6	0.3	0.5
Slovenia	0.7	0.3	0.5
Hungary	0.9	0.3	0.6
Romania	0.4	0.1	0.3
Poland	0.3	0.1	0.2
Slovakia	0.3	0.1	0.2

120). This is explained by a long-lasting latent period from the time of exposure to asbestos to the manifestation of the disease, which is from 20 to 40 years. The disease is significantly more frequent in males than in females because industries, in which asbestos is used, such as shipbuilding, cars and construction, employ mostly men. The sex ratio M:F in the world and in Croatia is 3–4:1. Only a small number of the patients suffering

form mesothelioma has the disease at a localized stage. According to the autopsy reports in literature, 30–50% of mesotheliomas metastasize either into regional lymph nodes or into distant organs¹¹. In Croatia in the period from 1989 to 1998 29% of mesotheliomas metastasized into regional lymph nodes or distant organs. According to the reports in literature mean survival of the patients is 9–12 months while at a more favorable stage it is 18 months. Survival depends on the type of mesothelioma. According to the WHO classification, mesotheliomas are divided into epithelial, sarcomatoid and mixed with the predominance of the epithelial or sarcomatoid. The longest mean survival with the epithelial type is 15 months, with the predominant epithelial type it is 13 months and with the sarcomatoid type it is 12 months.

The right strategy for the decrease of the incidence of mesothelioma and mortality from it is prevention. The most efficient prevention is the substitution of asbestos in industry with other materials, which is already under way in Western Europe.

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EPIDEMIOLOGIJA MALIGNIH PLEURALNIH MEZOTELIOMA U HRVATSKOJ U RAZDOBLJU OD 1989. DO 1998. GODINE

S A Ž E T A K

Maligni pleuralni mezoteliomi su rijetki tumori. Njihovo nastajanje povezuje se s ekspozicijom azbestu. Azbest ima široku primjenu kako u industriji tako i u predmetima svakodnevne upotrebe. U Hrvatskoj je stopa incidencije u razdoblju od 1989. do 1998. godine iznosila 0.4–1.1 / 100,000. Najveća stopa incidencije je u Istarskoj (2.9 / 100,000) i Splitsko-Dalmatinskoj županiji (2.5 / 100,000). Znatno je učestaliji kod muškaraca nego kod žena u omjeru 3.2:1. Rijetko se javlja prije 40. godine života, a najveći broj oboljelih je stariji od 65 godina. Oko 12% malignih pleuralnih mezotelioma metastazira u regionalne limfne čvorove, a 17% u udaljene organe. Bolest neminovno vodi smrti i prema podacima u Hrvatskoj u razdoblju od 1989. do 1998. godine mortalitet i incidencija su veoma blizu.