



MULTIPLE MYELOMA: FOCUS ON INTERNATIONAL EPIDEMIOLOGY LITERATURE

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Abstract: The aim of this review article is to focus on the global epidemiology of multiple myeloma presented in international literature. It focuses on the burden of multiple myeloma among patients, the rising percentages seen in the last few years and its risk factors. We included case reports, systematic analysis and prospective studies that deal with this rising issue.

INTRODUCTION

Multiple myeloma is a rare cancer among both sexes. It represents approximately 1% of all cancers and approximately 10% of haematological malignancies.(1) The etiology is poorly understood. It presents increasing interest due to its uprising frequency both in young and elderly patients.

The new therapeutic methods have significantly increased patients' life span. The mean age of diagnosis is between 50 and 70 years of age and the mortality is around 4-5/100 000/year. Thus, only 18% of the patients are under 50 years old at the moment of diagnosis and only 3% of the patients are younger than 40 years. The disease is more common in men than in women, males being accounted by 4,7/100000 and females 3,3/100000.(2)

In Romania, around 700 cases are registered each year, most young patients being around 28 years old.

In 2016, in the USA, the American Cancer society registered around 30330 new multiple myeloma cases. The Afro-American population is at a higher risk than the Caucasians, with a mean average of 2:1. It is rarer among the Asian population, with an incidence of 1-2 cases/100000 people.(3)

The etiology of multiple myeloma is poorly understood. It includes life style factors like obesity, diet, use of hormonal therapy, use of alcohol and tobacco. Other factors are related to the occupation and environment of the patient. These factors include agriculture and farming, pesticides, organic solvents, radiation, hair colouring products exposure, working in the cosmetic or hair-dressers industry.

Other factors can include: chronic immune stimulation or autoimmune pathology, family history, genetic variation, monoclonal gammopathy of undetermined significance.(4)

The purpose of this review article is to highlight new findings regarding multiple myeloma etiology and epidemiology. It also brings into focus the increasing rise of multiple myeloma incidence both worldwide and among young patients.

LITERATURE REVIEW

For this article we reviewed a series of prospective multinational studies, updates of clinical risks, disease

management and diagnosis, reviews of epidemiological and etiology literature, multi-centre international studies.

Multiple myeloma was the second most common hematologic malignancy in the USA in 2018.

A Systematic Analysis for the Global Burden of Disease Study 2016 related to multiple myeloma concluded that the 3 world regions with the age-standardized incidence rate of multiple myeloma were Australasia, North America, and Western Europe. Multiple myeloma was responsible for 98 437 (95% UI, 87 383-109 815) deaths globally with an age-standardized death rate of 1.5 per 100 000 persons (95% UI, 1.3-1.7).

From 1990 to 2016, multiple myeloma incident cases increased by 126%, and deaths increased by 94%. Among the regions, the largest increase in incident cases from 1990 to 2016 was seen in East Asia (China, North Korea, and Taiwan), with a rise of 262% (from 4760 in 1990 to 17 218 in 2016). Most deaths occurred in Western Europe (22 060; 95% UI, 17 571-25 628), high-income North America (15 894; 95% UI, 14 059-19 364), and South Asia (11 187; 95% UI, 8975-12 182). The countries with the most incident cases and deaths were the United States (24 407 incident cases and 14 212 deaths), China (16 537; incident cases and 10 363 deaths), and India (8 940 incident cases and 8 715 deaths).(6)

It is believed that by 2027 the global incidence of multiple myeloma will rise. According to Global Data the most affected countries will be China and USA. People who are younger than 35 account for approximately 1% of newly diagnosed cases each year. The most majority are over 65 years old. If new therapies were developed especially for elderly patients, the survival rate would significantly improve.(10)

According to a study published in 2016 concerning the global burden of multiple myeloma, multiple myeloma was responsible for 98 437 (95% UI, 87 383-109 815) deaths globally with an age-standardized death rate of 1.5 per 100 000 persons (95% UI, 1.3-1.7). The rate of incident cases increased by 126%, and deaths increased by 94% from 1990 to 2016. The highest rise from 1990 to 2016, of 262% was seen in China, North Korea and Taiwan.

The 3 world regions with the highest age standardized incidence rate of multiple myeloma were Australasia, North

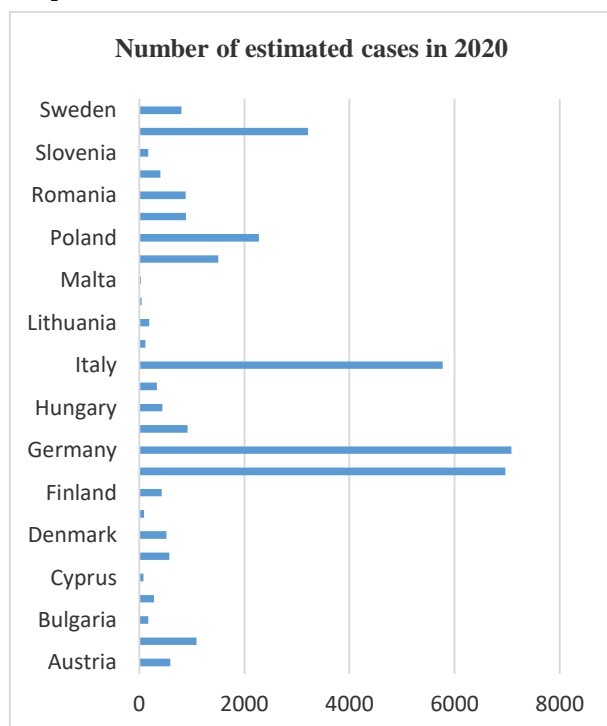
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America, and Western Europe.(11)

A study from 2016 concerning incidence and mortality of multiple myeloma in China, 2006–2016 concluded that in 2016 China had 16,500 new cases and 10,300 deaths of multiple myeloma. The incidence increased significantly from 2006 to 2016, while the mortality increased from 2006 to 2014, and remained stable from 2014 to 2016. The mortality rate was higher among males than females. Developed provinces had a higher rate of incidence and mortality.(12)

Figure no. 1. Multiple Myeloma estimated incidence in Europe in 2020 (13)



According to the European Cancer Information System, the European countries with the highest incidence in 2020 are Germany (7083 cases) and France (6967 cases), while Romania has an estimated 881 cases of multiple myeloma in 2020.

It is estimated that the countries least affected by this illness were Malta- 28 cases, Luxemburg- 44 cases and Cyprus-77 cases.

According to the European Cancer Information System, young people are less affected by this illness. An estimated number of cases in 2020 revealed the countries with most people under 40 affected by this illness are France- 42 cases, Germany- 31cases, Italy- 35 cases and Spain- 32 cases, while in Romania there were an estimated 16 cases of patients under 40 diagnosed with multiple myeloma.

Lifestyle factors have a proven impact on the epidemiology of multiple myeloma.

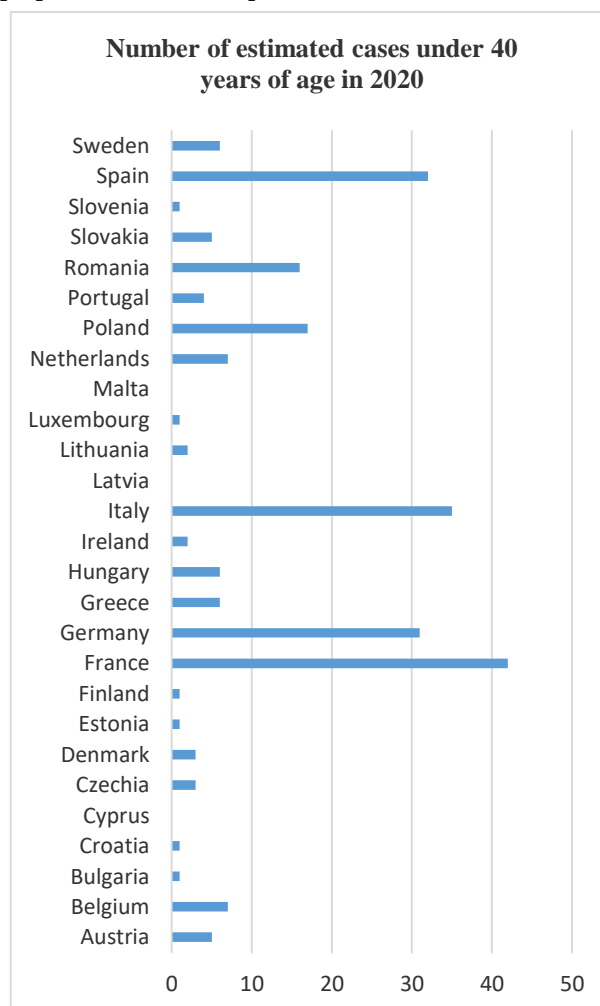
In a study conducted in California, common clinical conditions were examined as predictor factors for different types of cancers in 143574 patients. 14388 patients suffered from obesity and in 21 years, there were 33 cases of multiple myeloma diagnosed, among them standardized morbidity ratio=1.55, 95 percent confidence interval [CI]=1.06–2.17).(14).

Other lifestyle factors such as diet, tobacco and alcohol consumption or reproductive and hormonal factors have not yet been linked to developing multiple myeloma in the following years.

Other factors that should be taken into account are

occupational factors.

Figure no. 2. Multiple myeloma estimated incidence in people under 40 in Europe in 2020 (13)



It is proven that people who work in agriculture and farming have a lower risk of developing cancers per general, including multiple myeloma. This is due to their healthy life style.(14)

Pesticide use has not been proven in the past as being a risk factor. But a study in 2016, that included American and Canadian patients showed a link between the use of carbaryl, captan and DDT.(15)

The role of organic solvents is not yet well proven. A study published in 2010 exposures to certain chlorinated solvents may be associated with increased incidence of multiple myeloma. While results were less clear, exposure to 1,1,1-trichloroethane, methylene chloride, perchloroethylene, carbon tetrachloride, and chloroform conferred increased risk of multiple myeloma.(16)

According to SEER Cancer Statistics Review that includes statistics from 1975 through 2014 other risk factors for multiple myeloma are race; multiple myeloma is more frequent in Afro-American in USA than in Caucasians men, having a family history of multiple myeloma makes it more probable for a person to get this illness. Patients who suffer from monoclonal gammopathy of undetermined significance or solitary plasmacytoma have a higher risk of developing multiple myeloma than the rest of the population.(17)

Although the rising rates of multiple myeloma are a clear fact in the last few years, we cannot say the same thing

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about the risk factors. Some are well documented in multiple studies, while some still remain uncertain, more studies being needed to prove their role in this malignancy.

CONCLUSIONS

Multiple myeloma is a rare haematological malignancy worldwide. It is considered an illness of old people, although young patients can also be affected.

The regions with the highest incidence rate of multiple myeloma are Australasia, North America, and Western Europe. The highest incidence in Europe is in Germany, France and Italy, with people under 40 being rarely diagnosed.

Risk factors are frequently discussed in international literature, but many still need more evidence to be taken into consideration.

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