

Multiple myeloma: burden of disease analysis in some countries of Latin America (Mieloma múltiple: análisis de carga de la enfermedad en algunos países de Latinoamérica)

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Resumen

En Latinoamérica no existe información sistematizada para determinar/monitorizar el mieloma múltiple. El objetivo del estudio fue estimar la carga anual de enfermedad del mieloma múltiple en cinco sistemas de salud latinoamericanos mediante el número de pacientes atendidos, hospitalizaciones y muertes específicas, por grupo de edad.

Utilizando registros específicos codificados por CIE-10: C90 de bases de datos de los Sistemas Nacionales de Salud de Argentina, Colombia, Perú, Ecuador y Venezuela, obtuvimos y analizamos datos de 2015 (año completo) para pacientes atendidos y hospitalizados estratificados por grupo etario y para muertes específicas.

En 2015, el número total de casos atendidos (prevalencia de casos atendidos) fue: Argentina 1.278 (2.96), Colombia 875 (1.82), Ecuador 311 (1.91), Perú 603 (1.94) y Venezuela 758 (2.48); ≥ 50 años, representaron en promedio para los cinco países 86.88% (81.94% - 91.83%) del total. Los casos hospitalizados fueron (tasa promedio de hospitalización): Argentina 1.002 (1.31), Colombia 639 (1.51), Ecuador 218 (1.48), Perú 452 (1.52) y Venezuela 559 (1.34); en promedio ≥ 50 años, representaron 86.21% (80.12%-92.29%) del total. La hospitalización de ≥ 60 años vs. 50-59 años (62.86% [53.20% - 72.52%] vs. 23.35% [18.67%-28.03%]) aumentó ~ 2.7 veces, y esta población (≥ 60 años) se espera aumente $\sim 41\%$ para 2025. La tasa de mortalidad promedio fue 1.28 [0.82-2.62]. El mieloma múltiple representa una carga para la salud de los adultos mayores y los sistemas de salud, y se espera aumente conforme envejece la población.

Palabras clave: mieloma múltiple, prevalencia, hospitalización, mortalidad, base de datos, registros

Abstract

In Latin America, there is no systematic information to determine and monitor multiple myeloma. The objective of this study was estimate the annual burden of multiple myeloma disease in five Latin American healthcare systems through the number of attended patients, hospitalizations and specific deaths, by age group.

Using specific ICD-10:C90 coded registries from National Healthcare Systems' databases of Argentina, Colombia, Peru, Ecuador and Venezuela, we retrieved/analyzed 2015 complete year data for: attended and hospitalized patients stratified by age groups, and for specific deaths.

In 2015, the total number of cases attended (prevalence of cases attended) was: Argentina 1.278 (2.96), Colombia 875 (1.82), Ecuador 311 (1.91), Peru 603 (1.94) and Venezuela 758 (2.48); ≥ 50 years, represented on average for the five countries 86.88% (81.94%-91.83%) of total. Hospitalized cases were (average hospitalization rate): Argentina 1.002 (1.31), Colombia 639 (1.51), Ecuador 218 (1.48), Peru 452 (1.52) and Venezuela 559 (1.34); on average ≥ 50 years, represented 86.21% (80.12%-92.29%) of total. Hospitalization for ≥ 60 years vs. 50-59 years

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(62.86% [53.20%-72.52%] vs. 23.35% [18.67%-28.03%]) increased ~2.7 times, and this population (≥ 60 years) is expected to increase ~41% by 2025. Average mortality rate was 1.28 [0.82-2.62]. Multiple myeloma represents a burden on the health of elderly population and healthcare systems, and is expected to grow as the population ages.

Key words: multiple myeloma, prevalence, hospitalization, mortality, database, registries

Introduction

Multiple myeloma (MM) is a malignant neoplasm, which represents in the United States 1.8% of all cancers, and approximately 15% of the total hematological malignancies¹. It is most often diagnosed between 65-74 years of age, with a median age of 69 years¹. The American Cancer Society estimates that there were 30.330 new cases of this neoplasm in 2016, as well as 12.650 specific deaths during the same period¹. In the previous decade is documented an annualized growth of 0.8% for the incidence, together with a reduction of 0.8% in mortality per year (2004-2013), explained by the advent and availability of more effective therapeutic options¹.

Despite the decreasing mortality, MM is not yet considered a curable disease, although there is a lot of research and progress in the therapeutic options¹.

In Latin America in general, there is no systematic population-based information to determine and monitor the behavior of the incidence and prevalence of this condition. Based on this, the specialized local literature usually refers to the information coming from the US, or to the estimates made by the World Health Organization (WHO) for the different countries²⁻⁴. Although the estimates generated by the WHO are prepared from information provided by the countries themselves, this often corresponds to different periods and is mostly concentrated in specific mortality data, and only in some countries includes information of regional registers of population-based incident cases^{5,6}. Consider the information is no more than indicative of the behavior of the condition, but does not allow to delve into more details that reveal or at least outline more reliable elements to understand, analyze and compare the burden of disease for both, national healthcare systems as well as for the societies of these countries. This is relevant and of interest, in the case of a condition with a high concentration in the groups of older adults, above all, because the vast majority of the countries of Latin America are in full demographic transition in their respective population pyramids, with a clear phenomenon of «aging of the population»⁷⁻¹⁴.

It feels that, given the vulnerability of older adults in general with respect to their health, as well as the significant consumption of health resources that demand the cancer as a group of diseases, the MM should be analyzed and monitored in order to better understand the public health burden that it can represent.

However, as already mentioned, there is little systematic and reliable information on the prevalence, healthcare resources consumption and mortality by MM in Latin America.

Therefore, the aim of this study was to estimate the burden of disease, the utilization of certain healthcare resources, and the specific mortality of MM during a complete year, in Argentina, Colombia, Ecuador, Peru and Venezuela for 2015.

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Materials and methods

For the construction of the epidemiological and patient care data (inpatients and outpatients), a retrospective analysis of local data sources was conducted to estimate the burden of disease of MM in Argentina, Colombia, Ecuador, Peru and Venezuela among adults. Data were stratified by age groups of <20, 20 to 29, 30 to 39, 40 to 49, 50 to 59 and ≥ 60 years, to communicate the prevalence rates of patient care (inpatients and outpatients), as well as the total reported deaths for this cause, and in this way, to recognize the total annual burden of disease in each country. The information corresponds to the year 2015.

To obtain MM cases attended within one year (2015) in the different healthcare systems of these countries in general, and specifically regarding hospitalization and mortality reported from this cause, specific databases and queries of reported MM cases were used in each country, using as search criteria the cases reported in 2015 by ICD-10 code C90.0, gender and age group.

Given that MM is not a disease of mandatory reporting in any of these countries, despite periodic epidemiological data availability in some parts (regional population-based incidence registries), it was not possible by this means to gather information to estimate the incidence of ICD-10: C90. In addition, the ICD-10: C90 coded registries of medical care of the patients that were consulted from the databases within the healthcare systems, do not distinguish whether if the patient is new or a subsequent survivor, and as to this, it was not possible to obtain information that supports the construction of a rate of incidence of the condition.

In order to obtain both the cases attended in general and specifically the inpatients information, the consulted data sources were different health agencies for each country, which were requested the specific relevant information (e.g. Ministerio de Salud Pública (MSP), *Manejo de Hospitales Públicos*, *Instituto Nacional de Cancerología*, *Egresos hospitalarios según establecimientos de salud por causa específica* (CIE-10: C90)¹⁵⁻³⁵.

The specific and updated population pyramid for 2015 (by gender and age groups) for each country, was obtained from official sources corresponding to the census or population counts, as well as the official current population projections in each analyzed country⁷⁻¹⁴.

Since neither epidemiological studies, nor population-based up-to-date registries in which the patient is followed clinically for a certain period, are available systematically for this diagnosis in the different analyzed countries, it was decided to estimate a surrogate prevalence of MM with a proxy variable.

The information taken as this proxy variable was the total number of patients with MM (ICD- 10: C90.0) that were attended for a full year (2015), in the respective healthcare system in each analyzed country, based on the fact that it could be standardized, and thus compared among the different countries, as well as in different periods in the timeline. In accordance with this, an estimation of the prevalence of attended cases of MM in a year, in each of the countries was prepared. The prevalence was calculated on the basis of the total number of cases of MM (ICD-10 code C90.0) registered as attended in the above-mentioned databases sources during 2015¹⁵⁻³⁵ both for hospitalized patients, as well as non-hospitalized patients. The data was collected within age groups (<20, 20 to 29, 30 to 39, 40 to 49, 50 to 59 and ≥ 60 years), and then it was divided into the population/100.000 inhabitants, respectively for each age group, to obtain the prevalence rate of patients attended in the healthcare system for 100.000 people-year and by specific age group, both in general and specifically for in patients (hospitalized patients) and outpatients.

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The total number of deaths due to the ICD-10 code C90.0 was obtained from the data published by local official sources in each country. The total number of deaths reported from MM in accordance with the ICD-10, was divided into the total population/100.000 inhabitants, to estimate a general mortality rate from MM for each country for 2015³⁶⁻⁴¹.

Results

In 2015, in general, the total number of cases attended with MM ICD-10: C90 in the respective healthcare systems (prevalence of cases attended = cases/100.000 inhabitants) in some countries of Latin America was the following: in Argentina 1.278 (2.96), Colombia 875 (1.82), Ecuador 311 (1.91), Peru 603 (1.94) and Venezuela 758 (2.48) (Table 1). As to hospitalized cases (average hospitalization rate per inpatient case = number of hospitalizations in one year/number of yearly inpatients): Argentina 1.002 (1.31), Colombia 639 (1.51), Ecuador 218 (1.48), Peru 452 (1.52) and Venezuela 559 (1.34).

MM average mortality rate (mortality rate = deaths from MM/100.000 total inhabitants) of the five countries reported in 2015 was 1.28 (CI 95% 0.60-1.95), with a range of 0.82-2.62 (Table 1).

Regarding the distribution of the number of cases attended, it can be seen that this increase in a similar way in each country, according to each age category increases too. A very similar dynamic can be seen in the number of hospitalized patients.

Table 1. Multiple myeloma: attended, hospitalized patients and deaths in one year, from five countries in Latin America, 2015

	Argentina	Colombia	Ecuador	Peru	Venezuela
Attended patients	1278	875	311	603	758
Hospitalized patients	1002	639	218	452	559
Hospitalizations	1313	967	323	688	750
Deaths	622	424	133	286	384
Rates					
Patients (x100.000 inhabitants)*	2.96	1.82	1.91	1.94	2.48
Hospitalizations (x̄ x patient/year)**	1.31	1.51	1.48	1.52	1.34
Mortality (x 100 000 inhabitants)***	2.62	0.88	0.82	0.82	1.25

*Patients attended x 100.000 inhabitants-year

**Hospitalizations average x hospitalized patient-year

***Specific mortality x 100.000 inhabitants-year

Analyzing the highest concentration of cases attended by age group, it can be easily seen that the group of age ≥50 years, represents on average for the five countries observed the 86.88% (CI 95% 81.94-91.83) of the total number of cases of the prevalence of attention. With regard to hospitalized patients, we also see a large concentration in this

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age group (86.21% [CI 95% 80.12-92.29]). Specifically, the patients aged ≥ 50 years attended (% of the total number of patients attended) by country were: Argentina 1.063 (83.18), Colombia 794 (90.74), Ecuador 280 (90.03), Peru 475 (78.77) and Venezuela 695 (91.69). With regard to hospitalized patients of the same age group, when reviewed by country, the dynamics are very similar to that observed for patients attended in general (Table 2).

In general terms, it can be seen that the proportion of cases of hospitalization for patients of 50-59 years when compared with the group of age ≥ 60 years, increased significantly with age. In the age group of 50-59 years, the rate of hospitalization accounted for an average of 23.35% (CI 95% 18.67-28.03) of the total number of attended, while for the group of age ≥ 60 years, this rate was 62.86% (CI 95% 53.20-72.52), that is to say, an increase of ~ 2.7 times (Table 2).

Table 2. Multiple myeloma: distribution of attended and hospitalized patients by age group in one year from five countries in Latin America, 2015

Country	Age Groups					
	<20 years	20 to 29 years	30 to 39 years	40 to 49 years	50 to 59 years	≥ 60 years
Argentina						
Attended patients	2	13	57	143	424	639
%	0.17%	1.02%	4.43%	4.43%	33.14%	50.08%
Hospitalized patients	1	4	22	106	302	567
%	0.10%	0.41%	2.24%	10.56%	30.15%	56.54%
Colombia						
Attended patients	2	4	12	63	127	667
%	0.25%	0.51%	1.40%	7.19%	14.35%	76.30%
Hospitalized patients	2	3	7	46	114	467
%	0.38%	0.53%	1.11%	7.22%	17.82%	72.94%
Ecuador						
Attended patients	2	1	8	20	44	236
%	0.51%	0.36%	2.42%	6.57%	14.07%	76.07%
Hospitalized patients	1	1	4	38	50	124
%	0.50%	0.63%	1.64%	17.35%	23.15%	56.73%
Peru						
Attended patients	5	7	33	83	188	287
%	0.89%	1.24%	5.43%	13.77%	31.13%	47.54%
Hospitalized patients	3	3	12	78	123	233
%	0.61%	0.70%	2.64%	17.35%	27.15%	51.54%
Venezuela						
Attended patients	2	3	9	49	126	569
%	0.20%	0.34%	1.17%	6.46%	16.62%	75.20%
Hospitalized patients	1	2	4	22	104	426
%	0.18%	0.39%	0.77%	4.02%	18.61%	76.02%

If we concentrate specifically in the age group of ≥ 60 years, the figures of both prevalence of cases attended (cases attended ≥ 60 years/ total population aged ≥ 60 years), as well as hospitalized cases (cases hospitalized ≥ 60 years/ total population aged ≥ 60 years), increases significantly. The average of the five countries in the prevalence of cases attended corresponds to 13.16 (CI 95% 9.72-16.60), and of hospitalized patients is of 9.47 (CI 95%

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7.05-11.89). This is a very relevant finding of the analysis, since according with the population official agencies' projections, the population growth of the group of ≥ 60 years, will be on average of 41.7% (CI 95% 31.4-52.0) for 20259-16, and this population is known internationally, to be the one with the highest incidence and prevalence rates¹ (Table 3).

Table 3. Multiple myeloma: patients ≥ 60 years attended and hospitalized in one year from five countries in Latin America, 2015

	Argentina	Colombia	Ecuador	Peru	Venezuela
Attended patients	639	667	236	287	569
Hospitalized patients	567	467	124	233	426
Rates					
Patients (x100.000 inhabitants)*	9.96	12.50	14.69	9.53	19.12
Hospitalized Patients (x 100.000 inhabitants)**	8.84	8.75	7.72	7.74	14.31

*Attended patients ≥ 60 years x 100.000 inhabitants ≥ 60 years-year

**Hospitalized Patients ≥ 60 years x 100.000 inhabitants ≥ 60 years-year

Discussion

Multiple myeloma is a relatively infrequent neoplasia, it has been reported that represents about 1% of total cancer, and close to 15% of total hematologic cancer¹. However, in countries where there is systematic and current epidemiological information, there has been an increase in the incidence and prevalence of this disease in recent times, particularly among older adults (>60 years)¹. Despite recent therapeutic advances, the condition continues to show high lethality and is not considered a curable disease¹.

As it was expected, according to the international literature¹, increasing age was associated with a substantial increase in the prevalence of patients with MM (ICD-10: C90) attended in the national healthcare systems, also increasing the likelihood of hospitalization for this cause. In the United States in 2009, there were 18.200 hospital discharges for ICD-10: C90 as a primary diagnosis among adults (1.49% of all hospitalizations by cancer as a primary cause in the year, and 18.6% of the hematologic malignancies as the primary cause of 2009)⁴². Recently, in the medicare population, which is 92% ≥ 65 years, 2.765 (65.1%) of newly diagnosed patients with MM were hospitalized during the first year, with an incidence rate of 151.8/100 patient-years, information with similarities with ours. Patients with a history of chronic heart conditions and kidney failure, showed the highest numbers⁴³.

In this regard, MM can impose significant financial costs due to the high rate of hospitalization, the specific treatment that involves both bone marrow transplant and chemotherapy¹, and by the loss of productivity due to presumably premature death or disability.

Administrative healthcare databases (outpatient, inpatient, hospital discharges, diagnostic tests, procedures, etc.), have been in use for several years, both in America and Europe⁴⁴. These have been used to strengthen, validate, or even as an attempt to replace the population-based epidemiological registries, specifically in cancer for monitoring

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purposes⁴⁵. Also, they have been used for administrative, public policies and for resources management purposes, among other uses⁴⁴.

Among the different administrative health databases, hospital discharges have been the most used⁴⁴. Recently, it was carried out a similar study in many countries as was our own. This study used the same methodology, analyzing hospitalization for pneumonia in the elderly population as information of morbidity and increased healthcare utilization⁴⁶. Other studies have applied ICD-based data as a measure of pneumonia disease burden in other parts of the world and have evaluated ICD-based pneumonia indicators over time as a metric for monitoring pneumococcal vaccine impact⁴⁶.

Administrative healthcare databases, have strengths that enable them to be for various uses, such as those mentioned above. In addition, they are relatively inexpensive and easy to obtain and use when compared with the cost and time invested to obtain the same data through surveys or clinical records abstraction; also they are more reliable than other data sources, such as self-reported patients outcomes, or doctors' round tables, that in general represent their specific experience with regard to the surveillance of the disease and the resources consumption; besides, they are generally available for several years, allowing the analysis of trends. In addition, due to its coverage of large populations, they can be used for the analysis of concrete facts or subgroups of the population. Despite these considerable advantages, there are also weaknesses that can limit their usefulness for certain applications. Some of them are the differences in the methods and policies for gathering information among health systems and countries, compromising the comparability of the databases; and also, in many cases, the clinical and therapeutic information is not detailed enough and robust. These weaknesses are importantly minimized, using standardized and universally accepted classifications, such as ICD 10 today, and by initiatives in some parts of the world, to increase and improve the quality of the data available in the databases registries⁴⁴.

In this specific case, we consider that the analysis of the attended and hospitalized cases through their identification by the ICD 10 coding (ICD 10: 90.0), can be functional as a proxy variable of the disease prevalence, allowing the metrics of different healthcare resource consumption, and most importantly, facilitating the analysis of trends in the behavior of the condition, for decision-making in the approach of Multiple Myeloma in the Latin American environment.

Further research into the validation of administrative coded cancer and other diseases in Latin America with regard to cause and therapeutic resources usage, would significantly benefit our understanding of the nature of various clinical conditions in adults, specifically in the elderly population.

Bearing in mind that in accordance with the official national agencies in each country⁷⁻¹⁴, the population growth of the group of ≥ 60 years, will be on average of $>41\%$ for 2025, and that this population is known internationally, to be the one with the highest incidence and prevalence rates of MM¹. If we assume the same behavior of the disease within the five analyzed countries, for the year 2025 there would be an increase in the number of hospitalizations $>22\%$ for the population ≥ 60 years of age, a fact that undoubtedly marks a significant burden for the respective healthcare systems. As shown, MM, within the hematologic malignancies represents a burden on the health of the elderly population, which can continue to grow as the population ages also representing a burden on healthcare systems as well.

Acknowledgements: We thank Links&Links for the support in conducting the research as well as for the medical

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writing assistance, both funded by Takeda Pharmaceuticals.

Conflicts of interest: This study was undertaken with the financial support of Takeda Pharmaceuticals, without generating any type of legal commitment and/or related to the results. At the time of the study, Marcio Pineli, Carla Amigo, Carlos A. Alvarado, Rhadames Figueroa and Edwin Bucheli were employees of Takeda Pharmaceuticals. Links&Links provided support in conducting the research and medical writing assistance, both funded by Takeda Pharmaceuticals.

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