Contributions of a regional approach to document hematologic disease in Mexico: a 10-year experience in an open population

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ABSTRACT

Objectives: To demonstrate the importance of regional efforts to register features and report frequency of hematologic diseases in the context of incomplete national registries.

Methods: Frequencies and salient characteristics of hematologic diseases in Northeast Mexico were documented in a reference center at a tertiary care university hospital during the decade 2005–2015. Disease categories were grouped by age, sex and diagnosis. Age group distribution followed WHO guidelines in years as children (0–17), adults (18–64) and elders (+65).

Results: 2406 patients were included: 1239 (51.5%) were females and 1167 (48.5%) males; F:M ratio was 1.06:1; median age was 35 years (0–95). The frequency by age group included adults, 1370 cases (56.9%), children, 695 cases (28.9%), and elderly, 341 (14.2%). Most frequent diagnoses were acute lymphoblastic leukemia (ALL) 18.2% (n = 438), anemia 15.9% (n = 383), non-Hodgkin’s lymphoma (NHL) 15.7% (n = 378), immune thrombocytopenic purpura (ITP) 9.8% (n = 235) and Hodgkin’s lymphoma (HL) 6.5% (n = 156). Median age for the whole cohort was 35 years; for children, was 6 years, for adults 40 and for the elderly 73. Results for ALL, anemia and ITP were comparable to high-income countries; NHL, HL and chronic myeloid leukemia presented a decade earlier.

Discussion: Complete, opportune reliable information on the number of cases, age and sex distribution with the potential to influence strategies for timely diagnosis and treatment options for important hematologic diseases can be accrued by regional centers.

Conclusion: Information on hematology diseases derived of regional registries in low-middle income countries is a reasonable alternative to complement and update national registries.

Introduction

In low-middle income countries (LMIC), there is limited data regarding the frequency and age distribution of hematologic diseases. This group of pathologies is not easily documented due to lack of national registries, local underreporting and isolated efforts to document these relatively infrequent diseases. Hematologic diseases are customarily included in comprehensive oncology reports like GLOBOCAN 2008/2012 [1] and Cancer statistics [2]; in these databases, malignant hematologic diseases are among the most important cause of morbidity–mortality and benign pathologies are overlooked.

Globally, malignant hematologic diseases are responsible for approximately 7% of each estimated new cancer cases and deaths in Europe [1,3] and almost 10% in the United States during 2015 [2]. Benign hematologic diseases such as anemia are still some of the most important causes of disability worldwide. They had a global prevalence of 32.9% in 2010, accounting for 8.8% of total disabilities, causing over 68 million-years lived with disability [4].

The incidence of hematologic diseases is partially documented in Mexico; many reports are limited and pertain to individual diseases or single centers, halting the development of successful strategies to improve diagnosis and treatment at the national level. These strategies are of great importance against malignant diseases, which frequently develop in children and adults during academic and productive age; thus hematologic diseases represent a societal burden and affect the quality of life and income, given their severity and prognosis. In addition, new treatments are expensive and their use prolonged [5,6], making them difficult to afford in LMIC whose health budgets are restricted.

Leukemias were the seventh cause of death due to malignancy among individuals aged 20 years and older, accounting for 1259 deaths; 4.2% of total cancer deaths in Mexico during 2013 [7]. The frequency, age and sex of the patients with acute and chronic leukemias at two large centers in Mexico City were recently reported [8].

The frequencies and characteristics of open population, uninsured patients with hematologic diseases
in the Northeast region of the country were analyzed including all cases diagnosed during a 10-year period attending a hematology reference center of a tertiary care public institution in the State of Nuevo León, with a population close to five million, half of which have no medical insurance [9].

Material and methods
Clinical files and electronic databases of patients diagnosed with a hematological disease who attended the Hematology Department of the Dr. Jose E. Gonzalez University Hospital of the School of Medicine of the Universidad Autónoma de Nuevo Leon, in Monterrey, Mexico, between 2005 and 2015 were analyzed. The hospital provides health services for the open population in three States of the Northeast. Inhabitants in these States add up to 11.5 million, half of them uninsured. Age distribution in the population of the three neighboring Mexican Northeast States in the area of the study is as follows: 0–17 years, 3,110,000; 18–64 years, 7,400,000; ≥65 years, 970,000; females constitute 50.5% and males 49.5% [9]. Data including gender, age, specific hematologic diagnosis, comorbidities, signs and symptoms were documented. For the purposes of this study, patients were divided into three groups: children (0–17 years), adults (18–64 years) and elderly (≥65 years). A database was built incorporating the patient’s diagnosis and epidemiologic information. Data were analyzed using the statistical package SPSS v.21.

Results
Results are summarized in Tables 1–4. During the 10-year study period, 2406 hematology patients were registered, 1239 (51.5%) female and 1167 (48.5%) male, for an F:M ratio of 1.06:1; median age for the whole cohort was 35 years (0–95). The frequency by age group was higher in adults with 1370 cases (56.9%), followed by children in 695 cases (28.9%) and 341 (14.2%) in the elderly. The most frequent diagnoses were acute lymphoblastic leukemia (ALL, 18.2%), followed by anemia (15.9%), non-Hodgkin’s lymphoma (NHL, 15.7%), immune thrombocytopenic purpura (ITP, 9.8%) and Hodgkin’s lymphoma (HL, 6.5%). These five diseases compose 66.1% of the total. The remaining 33.9% corresponded to miscellaneous diagnoses (Table 1).

In the children’s group, there were 695 patients, 405 boys (58.3%) and 290 girls (41.7%), with an M:F ratio of 1.39:1. Median age was 6 years (0–17). The most frequent diagnoses were ALL (45.5%), ITP (12.5%) and anemia (5.9%), followed by others with lower frequencies (Table 2). The adult group consisted of 1370 patients, 603 men (44%) and 767 women (56%) with an F:M ratio of 1.27:1; median of age at diagnosis was 40 years (18–64). The most frequent disease was anemia (20.5%), followed by NHL (17.5%) and ITP (9.10%); 16 additional diagnostic categories with lower frequencies were found (Table 3). The elderly group included 341 patients, 159 males (46.6%) and 182 females (53.4%), with an F:M ratio of 1.14:1. Median age at diagnosis was 73 years (65–95). The most frequent diseases were NHL (32%), anemia (18.20%) and multiple myeloma (MM) (10.30%), followed by less frequent pathologies (Table 4).

Findings for more frequent diagnostic categories are discussed with respect to what is known in other populations in the next section.

Discussion
Data on frequency, sex and age distribution of hematologic diseases are scarce in many LMICs. We documented these important aspects over 10 years analyzing malignant and benign pathologies and report the relevant findings. Although our study has several limitations, it is the first study carried out in Mexico to gather all-age data on malignant as well as benign hematological diseases in a specific region and time period in a well-defined homogeneous segment of the open uninsured population.

The adult group predominated over children and the elderly. The most frequent diseases were ALL, anemia, NHL, ITP, HL, chronic myeloid leukemia (CML) and MM explaining over 75% of the cases. Findings for these diagnostic categories are discussed below.

Acute lymphoblastic leukemia
In northeast Mexico, ALL is the principal cause of death by malignant cancer in children and adolescents between 0 and 19 years, accounting for 48.5% of all cases [7]. We documented 437 patients with ALL in the study period with an M:F ratio of 1.1:1, slightly lower than 1.3:1 reported in the US [10] but the same as that found in the UK, 1.1:1 [11]. Median age was 10 years (0–79), five years younger than in the US [10]. In our children’s group, median age was 6 years (0–17), similar to other LMICs, with results between 5 and 6.4 years [12,13]. Recently, we defined survival rates for adult ALL patients [14], for children [15] and adolescents [16] as well as relapse and its outcomes in the pediatric group [17] over a decade. In an effort to bridge this critical information gap, we documented epidemiologic characteristics of over 1000 acute leukemia patients in five States of Mexico [18].

Median age in our adult ALL group was 31.5 years (18–64) with an M:F ratio of 1.2:1. Age of diagnosis in the US was reported to be almost 10 years older, at 40 years [19]. In a previous study in central Mexico, median age was 5 years younger than ours, 27 years [20], underscoring the biological and geographic
Table 1. Diagnosis and demographic characteristics of 2406 patients with hematologic diseases attending a reference regional center in Northeast Mexico between 2005 and 2015.

| Diagnosis                                | Gender                  | Total f (%) | Age, years median (%) |
|------------------------------------------|-------------------------|-------------|-----------------------|
|                                          | Male (%) | Female (%) | n = 2406       |                        |
| Acute lymphoblastic leukemia             | 323 (53) | 206 (47)  | 438 (18.2)       | 10 (1–79)              |
| Anemia                                   | 98 (25.5) | 285 (74.4) | 383 (15.9)       | 42 (0–91)              |
| Non-Hodgkin’s lymphoma                   | 222 (58.7) | 156 (41.3) | 378 (15.7)       | 53 (0–92)              |
| Immune thrombocytopenic purpura          | 92 (39.1) | 143 (60.9) | 235 (9.8)        | 25 (0–94)              |
| Hodgkin’s lymphoma                       | 95 (60.9) | 61 (39.1)  | 156 (6.5)        | 28.5 (0–81)            |
| Acute myeloid leukemia                   | 71 (51.8) | 66 (48.2)  | 137 (5.7)        | 34 (0–85)              |
| Chronic myeloid leukemia                 | 53 (52)   | 49 (48)    | 102 (4.2)        | 40 (2–81)              |
| Multiple myeloma                         | 48 (52.2) | 44 (47.8)  | 92 (3.8)         | 60 (25–87)             |
| Aplastic anemia                          | 29 (48.3) | 31 (51.7)  | 60 (2.5)         | 33 (1–72)              |
| Myeloproliferative neoplasm              | 29 (51.8) | 27 (48.2)  | 56 (2.3)         | 57.5 (1–88)            |
| Myelodysplasia                           | 23 (43.4) | 30 (56.6)  | 53 (2.2)         | 55 (0–95)              |
| Bleeding disorders                       | 41 (82)   | 9 (18)     | 50 (2.1)         | 16 (0–76)              |
| Autoimmune hemolytic anemia              | 16 (34.8) | 30 (65.2)  | 46 (1.9)         | 32.5 (1–82)            |
| Chronic lymphocytic leukemia             | 21 (53.8) | 18 (46.2)  | 39 (1.6)         | 62 (22–92)             |
| Hypercoagulable state                    | 17 (48.6) | 18 (51.4)  | 35 (1.5)         | 34 (7–78)              |
| Hemoglobinopathies                       | 14 (46.7) | 16 (53.3)  | 30 (1.2)         | 25 (0–76)              |
| Hereditary spherocytosis                  | 8 (28.6)  | 20 (71.4)  | 28 (1.2)         | 6.5 (0–38)             |
| Plasmacytoma                             | 4 (44.4)  | 5 (55.6)   | 9 (0.4)          | 54 (38–80)             |
| Evans’ syndrome                          | 4 (44.4)  | 5 (55.6)   | 9 (0.4)          | 29 (1–66)              |
| Paroxysmal nocturnal hemoglobinuria      | 3 (37.5)  | 5 (62.5)   | 8 (0.3)          | 2 (1–3)                |
| Miscellaneous erythroid lineage          | 25 (86.2) | 4 (13.8)   | 29 (1.2)         | 0 (0–49)               |
| Miscellaneous white lineage              | 21 (72.4) | 8 (27.6)   | 29 (1.2)         | 11 (0–75)              |
| Miscellaneous platelets                  | 1 (25)    | 3 (75)     | 4 (0.2)          | 39 (1–74)              |

heterogeneity of ALL. The deleterious effect of increasing age at diagnosis of ALL has been reported for our cohort [21].

Anemia

In 2015, the WHO estimated that approximately 50% of cases of anemia are due to iron deficiency (ID) [22]. The global prevalence of anemia is 27% and 1.93 billion people are affected, with developing countries accounting for 90% of the burden; 43% of preschool children and 29% women of reproductive age have anemia worldwide [22]. ID anemia is the dominant cause (62.6%). Anemia thus affects one in four persons globally.

In Mexico, the national prevalence of ID anemia in children <5 years was 23.3% and 10.1% in children aged 5–11 years with no gender difference. In adolescents between 12 and 19 years, the prevalence was 5.6%, predominant in girls, 70% vs. 30% in boys. Seventeen percent of pregnant women (12–49 years) and 11.6% of non-pregnant women had anemia. In the same study, the prevalence of anemia in the elderly was 16.5% [23]. Median of age at diagnosis of anemia in our study group was 42 years (0–91 years). In the children’s group (0–17), median age was 2 years with an F:M ratio of 1.4:1, while in the adult group, median age was 40 years with an F:M ratio of 3.2:1. Prevalence was similar between genders at a young age and higher in females at adult age [23]. Our highest

Table 2. Diagnosis and demographic characteristics of 695 children with hematologic diseases in Northeast México diagnosed between 2005 and 2015 in Monterrey, México.

| Diagnosis                                | Gender                  | Total f (%) | Age, years median (%) |
|------------------------------------------|-------------------------|-------------|-----------------------|
|                                          | Male (%) | Female (%) | n = 695       |                        |
| Acute lymphoblastic leukemia             | 167 (52.8) | 149 (47.2) | 316 (45.5)       | 6 (0–17)              |
| Immune thrombocytopenic purpura          | 47 (54)   | 40 (46)    | 87 (12.5)        | 8 (0–17)              |
| Anemia                                   | 17 (41.5) | 24 (58.5)  | 41 (5.9)         | 2 (0–17)              |
| Bleeding disorder                        | 34 (97.1) | 1 (2.9)    | 35 (5)          | 4 (0–17)              |
| Acute myeloid leukemia                   | 21 (63.3) | 12 (36.4)  | 33 (4.7)         | 7 (0–17)              |
| Hodgkin’s lymphoma                       | 23 (71.9) | 9 (28.1)   | 32 (4.6)         | 11 (0–17)             |
| Non-Hodgkin’s lymphoma                   | 18 (60)   | 12 (40)    | 30 (4.3)         | 8 (0–17)              |
| Hereditary spherocytosis                  | 7 (38.9)  | 11 (61.1)  | 18 (2.6)         | 4 (0–11)              |
| Aplastic anemia                          | 11 (78.6) | 3 (21.4)   | 14 (2)          | 8.5 (1–15)            |
| Hemoglobinopathies                       | 7 (70)    | 3 (30)     | 10 (1.4)         | 5 (0–14)              |
| Autoimmune hemolytic anemia              | 3 (37.5)  | 5 (62.5)   | 8 (1.2)          | 10.5 (1–17)           |
| Chronic lymphocytic leukemia             | 1 (16.7)  | 5 (83.3)   | 6 (0.9)          | 11.5 (2–15)           |
| Hypercoagulable state                    | 4 (66.7)  | 2 (33.3)   | 6 (0.9)          | 13 (7–17)             |
| Myelodysplasia                           | 1 (20)    | 4 (80)     | 5 (0.7)          | 9 (0–13)              |
| Myeloproliferative neoplasm              | 3 (75)    | 1 (25)     | 4 (0.6)          | 3.5 (1–15)            |
| Evans’ syndrome                          | 1 (50)    | 1 (50)     | 2 (0.3)          | 7.5 (1–14)            |
| Paroxysmal nocturnal hemoglobinuria      | 1 (100)   | 0 (0)      | 1 (0)           | 0 (0–9)               |
| Miscellaneous erythroid lineage          | 24 (85.7) | 4 (14.3)   | 28 (4)          | 3.5 (0–16)            |
| Miscellaneous white lineage              | 14 (77.8) | 4 (22.2)   | 18 (2.6)         | 3.5 (0–16)            |
| Miscellaneous platelets                  | 1 (100)   | 0 (0)      | 1 (0)           | 1                    |
prevalence was found in those aged between 0 and 4 and 35 and 45 years. We recently documented the need to provide targeted teaching regarding ID diagnosis and treatment for non-hematologists and first contact physicians in a general hospital [24].

### Non-Hodgkin's lymphoma

In a study from Mexico’s National Cancer Institute, 5083 new cases with 2815 deaths due to NHL during 2015 were censored [25]. We documented 378 patients with NHL in the study period with an M:F ratio of 1.4:1. Median age was 53 years and thus it occurred one decade earlier than in industrialized countries [26], but a decade later than 42.5 years in Pakistan [27].

NHL was the most frequent hematologic disease in the elderly, with a similar median age to previous studies [26]. It increases exponentially with age. In the UK, each year around half (49%) of NHL cases are diagnosed in people aged 70 or older [28], while more than 70% of cases reported in the US were in people aged 55 and older [10]. We found a younger median age, with most cases diagnosed around 40 years of age, 15 years earlier than in high-income countries. Usually, NHL is a disease of the elderly; however, we found an important frequency in the population in the 20s and 30s. NHL has been acknowledged as a major contributor to the early death of young adults in Canada, where it accounts for 11% of cancer diagnosed in young men, only second to testicular cancer, and it is an important cause of potential years of life lost for young men aged 20–44 [29]. In a recent study, we described advanced stages at diagnosis, younger age and low cure rate for NHL in our reference center, even after

### Table 3. Salient characteristics of 1370 patients in the adult group with hematologic diseases in Northeast México during 2005–2015.

| Diagnosis                        | Gender: male (%) | Female (%) | Frequency (%) | Age, years (median %) |
|----------------------------------|------------------|------------|---------------|-----------------------|
| Anemia                           | M: 60 (21.4); F: 220 (78.6) | 280 (20.5) | 40 (18–64)    |
| Non-Hodgkin’s lymphoma           | M: 142 (59.4); F: 97 (40.6) | 239 (17.5) | 47 (18–64)    |
| Immune thrombocytopenic purpura  | M: 37 (29.6); F: 88 (70.4) | 125 (9.10) | 37.5 (18–64)  |
| Acute lymphoblastic leukemia     | M: 65 (55.1); F: 53 (44.9) | 118 (8.6)  | 31.5 (18–64)  |
| Hodgkin’s lymphoma               | M: 66 (58.4); F: 47 (41.6) | 113 (8.3)  | 31 (18–62)    |
| Chronic myeloid leukemia         | M: 51 (54.8); F: 42 (45.2) | 93 (6.8)   | 40 (18–64)    |
| Acute myeloid leukemia           | M: 42 (47.2); F: 47 (52.8) | 89 (6.5)   | 37 (18–63)    |
| Multiple myeloma                 | M: 33 (57.9); F: 24 (42.1) | 57 (4.2)   | 54 (25–64)    |
| Aplastic anemia                  | M: 16 (40); F: 24 (60) | 40 (2.9)   | 35 (18–61)    |
| Myeloproliferative neoplasm      | M: 17 (50); F: 17 (50) | 34 (2.5)   | 51 (21–64)    |
| Autoimmune hemolytic anemia      | M: 8 (25); F: 24 (75) | 32 (2.3)   | 34 (18–63)    |
| Myelodysplasia                   | M: 14 (48.3); F: 15 (51.7) | 29 (2.1)   | 49 (21–64)    |
| Hypercoagulable state            | M: 12 (42.9); F: 16 (57.1) | 28 (2)     | 36.5 (21–64)  |
| Chronic lymphocytic leukemia     | M: 11 (47.8); F: 12 (52.2) | 23 (1.7)   | 55 (22–64)    |
| Hemoglobinopathies               | M: 7 (38.9); F: 9 (61.1) | 18 (1.3)   | 29 (20–63)    |
| Bleeding disorders               | M: 7 (53.8); F: 6 (46.2) | 13 (0.9)   | 28 (19–56)    |
| Hereditary spherocytosis          | M: 1 (100); F: 9 (90) | 10 (0.7)   | 22.5 (19–38)  |
| Paroxysmal nocturnal hemoglobinuria | M: 2 (33.3); F: 4 (66.7) | 6 (0.4)    | 38.5 (26–46)  |
| Plasmacytoma                      | M: 4 (66.7); F: 2 (33.3) | 6 (0.4)    | 44.5 (38–58)  |
| Evans’ syndrome                  | M: 2 (33.3); F: 4 (66.7) | 6 (0.4)    | 35.5 (18–61)  |
| Miscellaneous white lineage      | M: 5 (62.5); F: 3 (37.5) | 8 (0.6)    | 41.5 (18–59)  |
| Miscellaneous platelets          | F: 2 (100)       | 2 (0.1)    | 39 (27–51)    |
| Miscellaneous erythroid lineage  | M: 1 (100)       | 1 (0.1)    | 49 (27–51)    |

### Table 4. Characteristics of 341 elderly patients with hematologic diseases treated at a reference center in Northeast México between 2005 and 2015.

| Diagnosis                        | Gender: Male (%) | Female (%) | Frequency (%) | Age, years (median %) |
|----------------------------------|------------------|------------|---------------|-----------------------|
| Non-Hodgkin’s lymphoma           | M: 62 (56.9); F: 47 (43.1) | 109 (32)   | 73 (65–95)    |
| Anemia                           | M: 21 (33.9); F: 41 (66.1) | 62 (18.2)  | 74 (65–91)    |
| Multiple myeloma                 | M: 15 (42.9); F: 20 (57.1) | 35 (10.3)  | 75 (65–87)    |
| Immune thrombocytopenic purpura   | M: 8 (34.8); F: 15 (65.2) | 23 (6.7)   | 74 (65–94)    |
| Myelodysplasia                   | M: 8 (42.1); F: 11 (57.9) | 19 (5.6)   | 73 (65–95)    |
| Myeloproliferative neoplasm      | M: 9 (50); F: 9 (50) | 18 (18)    | 73.5 (66–88)  |
| Chronic lymphocytic leukemia     | M: 10 (62.5); F: 6 (37.5) | 16 (4.7)   | 71 (65–92)    |
| Acute myeloid leukemia           | M: 8 (53.3); F: 7 (46.7) | 15 (4.4)   | 79 (68–85)    |
| Hodgkin’s lymphoma               | M: 6 (54.5); F: 5 (45.5) | 11 (3.2)   | 68 (65–81)    |
| Aplastic anemia                  | M: 2 (33.3); F: 4 (66.7) | 6 (1.8)    | 68 (65–72)    |
| Autoimmune hemolytic anemia      | M: 5 (83.3); F: 1 (16.7) | 6 (1.8)    | 75 (67–82)    |
| Acute lymphoblastic leukemia     | F: 4 (100)       | 4 (1.2)    | 75 (68–79)    |
| Chronic myeloid leukemia         | M: 1 (33.3); F: 2 (66.7) | 3 (0.9)    | 78 (72–81)    |
| Plasmacytoma                     | F: 3 (100)       | 3 (0.9)    | 77 (66–80)    |
| Hemoglobinopathies               | F: 2 (100)       | 2 (0.6)    | 70.5 (67–76)  |
| Bleeding disorders               | F: 2 (100)       | 2 (0.6)    | 73 (70–76)    |
| Paroxysmal nocturnal hemoglobinuria | M: 2 (66.7); F: 1 (33.3) | 3 (0.9)    | 69 (67–75)    |
| Miscellaneous white lineage      | M: 2 (66.7); F: 1 (33.3) | 3 (0.9)    | 69 (67–75)    |
| Miscellaneous platelets          | F: 1 (100)       | 1 (0.3)    | 74 (27–51)    |
the addition of rituximab [30]. Recently, detailed data on NHL in Mexican children have been reported from the Instituto Mexicano del Seguro Social (IMSS) [31].

**Immune thrombocytopenic purpura**

We documented 87 children with ITP during the 5-year period, with an M:F ratio of 1.1:1, similar to that reported in the intercontinental study with an M:F ratio of 1.2:1 [32]. Our median of age at diagnosis was 8 years, higher than in the US, Turkey and intercontinental reports, where median age was 5–5.7 years [32].

There were 148 adults (over 18 years) with ITP, with an F:M ratio of 2.26:1, higher than the 1.5:1 ratio in the UK [33]. As reported, in this group, the incidence is greater in women but our median age was 42 years, one and a half decades earlier than in the UK, 59 years [33]. In another study from our country, median age was 36.8 years (1–90) with an F:M ratio of 1.98:1 [34].

No significant seasonal fluctuation in the incidence of ITP was found in our children between cold seasons (September–March), 48.3%, vs. warm seasons (April–August), 51.7% (P= .320). None of our patients presented intracranial hemorrhage.

**Hodgkin’s lymphoma**

It affects approximately 5000 new patients in Latin America each year [2], whereas in Mexico, 935 cases were reported in 2003 [35]. In a recent report from the National Cancer Institute in Mexico, 1677 new cases of HL with 675 deaths were documented during 2015 [25]. We recently reported data on HL patients in Northeast México, finding a high rate of refractory disease, advanced stages at diagnosis and decreased survival [36].

HL affects people of all ages with peaks around 30 and after 60 years of age with this being the most common cancer in young adults [37]. The first peak in our study was at 4–7 years vs. 6–10 years in India [38]. Our second peak was at 17–26 years, different from a previous report from our country of between 15 and 19 years [35], underscoring regional geographic heterogeneity.

We documented 156 HL patients, with an M:F ratio of 1.55:1 different from India at 2.6:1. Our median age was 28.5 years (0–81), similar to India 28.7 [38], but younger than other countries like Japan with 34 years [39] and a decade earlier than in the US with 39 years [10].

**Acute myeloid leukemia**

There is no precise information regarding the epidemiologic aspects of acute myeloid leukemia (AML) in Mexico, but 600 new cases were reported in 1998 [40]. AML increases with age, and its incidence varies from 2–3 per 100,000 in young people to 15–20 in the older population [41]. The risk of developing AML increases 10 times after reaching 30 years, from 1 to 10 cases per 100,000/year [42].

We have reported the general characteristics and survival rates for AML in our center [43] documenting 137 patients with AML over five years with an M:F ratio of 1.07:1 [43]. In the US, this ratio is higher in males 1.4:1 [10]. The median age in our group was 34 years (0–85), similar to a previous regional study with a median of 32 years [43]. In contrast, reports from the US and Europe found considerably higher medians of 67–69 years [2,10,44], almost 35 years older than our patients, attesting to the many epigenetic influences in this malignancy. In this respect, the adolescent and young adult AML group has particular characteristics requiring an intensified chemotherapy approach and early access to transplantation, as reported in our patients [45].

**Chronic myeloid leukemia**

We documented 102 CML patients with an M:F ratio of 1.08:1, whereas in other studies, male predominance was more notable; in Spain, the ratio was 1.4:1 and in the US 1.35:1 [46,47]. The median age at onset was 40 years (2–81), differing considerably from 64 years in the US [10]; thus CML is currently diagnosed almost 25 years earlier at our regional center in Northeast Mexico, again underscoring geographic variation in biologic expression of leukemic clones. In our population, the percentage of patients between 20 and 44 years was 54.1%, superior to 31.7% in another report [46]. Patients 40 years or younger corresponded to 61.8% in our study, this differs from the US where the majority of patients (73%) were in the >40 years group [47]; in the UK, 50% of CML cases are diagnosed in people aged 65 and over [48], thus contrasting significantly with our population. Important cultural and socioeconomic factors affect negatively adherence to treatment in CML as recently documented by our group [49].

**Multiple myeloma**

We documented 92 MM patients with an M:F ratio of 1.09:1; as cited in other articles [10,50]. The median age of onset was 60.5 years (25–87 years), similar to previous studies in Mexico [51], whereas the US and Sweden report a median of 69 and 70 years, almost 10 years older than our population [10,50]. In our group, 62% of patients were <65 years (25–64 years) and 38% were 65 or older (65–87 years). In other studies, most patients belong to the elderly group, and in the UK, 59% cases are diagnosed in people aged 70 and older [52].

Although there is no complete recent data on MM, a previous report on lymphoproliferative diseases in México found a lower frequency than in Caucasian
populations [53]. In a recent report, we compared the characteristics of MM patients from our open population, with no access to bortezomib, with those of insured individuals that received treatment with bortezomib [54].

As exemplified in this study, regional reports on frequency and distribution of hematologic diseases are important, particularly in LMIC, where consolidated, periodically updated information is not always available. These data are required for the design and implementation of successful strategies leading to an opportune diagnosis and timely and effective treatment of hematologic diseases, as well as for middle- and long-term health budget planning for resource allocation.

In conclusion, these findings underscore the importance of accruing detailed data for regional consolidated frequency analysis to define and map influences associated with specific hematologic diseases at the national level.

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