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A population-based study of the epidemiology and clinical features of adults with acute myeloid leukemia in Algeria: report on behalf of the Algerian Acute Leukemia Study Group

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BACKGROUND AND OBJECTIVES: In Algeria, the incidence of hematologic malignancies has been difficult to estimate for many years. Today, many hematological centers, including 14 university hospitals, have been developed in the entire north and have useful epidemiological data pertinent to acute myeloid leukemia (AML). We studied the incidence of AML and its subtypes, age distribution, geographic distribution and trends in the rate of diagnosis over the last 5 years in Algeria. Secondary goals were to study trends of referral of AML cases from various regions to specific centers to assess the needs for health infrastructure and change of current practices.

DESIGN AND SETTING: Retrospective analysis of nationwide survey of all adult cases of AML (>16 years) diagnosed between 1 January 2006 and 31 December 2010.

PATIENTS AND METHODS: A survey form was distributed to all departments of hematology at the 15 participating centers.

RESULTS: The 1426 cases of AML diagnosed during the study period represented an annual incidence of 0.91/100 000 persons with a male to female (M/F) ratio of 1:16 and a median age of 45 years (range, 16-82 years). Nationally, 20% of cases AML were diagnosed in the whole western region of the country, 47% in the central and 33% in the east. There was a trend of continuous increase in the rate with age and in the rate of diagnosis over the last 5 years. The most common subtype was M2, followed by M4 and M5.

CONCLUSION: An overall increase in the number of AML patients diagnosed nationwide over the last five years indicates a need for additional health care resources including curative and therapy-intense strategies, such as stem cell transplant facilities to optimize outcome. The relatively younger age of patients compared to the Western countries may be due to the demographic composition of our population.

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In Algeria, the incidence of various hematologic malignancies has been difficult to estimate for many years due to insufficient number of hematological centers in a country covering an area of over two million square kilometers. Today, many hematological centers, including 14 university hospitals, that have been developed in the entire north, are reasonably distributed from east to west and have useful epidemiological data pertinent to acute myeloid leukemia (AML). This has allowed better access of patients for earlier diagnosis and comprehensive care and better registration of valuable epidemiological data with subsequent studies on many hematologic malignancies.[1-5] The national health system is based on free health care. Expenses are sponsored by a budget covered by the Ministry of Health and the social security office, and hematologic malignancies represent a significant part of this budget. In this context, an epidemiological study on AML in adults was conducted to determine its frequency and its clinical and financial impact, in order to assess the need for further development of institutional infrastructure or re-allocation of public health resources.

PATIENTS AND METHODS

We studied the incidence of adult AML, its subtypes, age and geographic distribution in Algeria and the trends in the rate of diagnosis over the last 5 years (from 1/1/2006 to 31/12/2010). Secondary goals included the study of pattern of referral from various regions to specific centers in order to assess the need for health infrastructure and change of current practices. A survey was distributed to all departments of hematology at the 15 centers distributed across the country. These centers represent all the institutions where AML patients are referred (see list at end of article).

Patients were identified according to their age, sex, date of presentation and area of residency. All patients aged 16 years or older with de novo AML were included. The diagnosis of AML was according to the World Health Organization (WHO) recommendations,[6] after analysis of the blood smears, the bone marrow aspiration, cytochemistry and flowcytometry for immunophenotyping of blast cells. Subtypes of AML were grouped according to the French/American/British (FAB) group classification.[7] Data on antecedent hematological disorder or previous chemotherapy or radiotherapy were not included.

We estimated the overall median age for all patients and for each sex. We estimated crude incidence rates per 100 000 with 95% confidence intervals (95% CI). We also estimated incidence according to age at diagnosis, grouped into 7 categories: 16-20, 21-39, 40-49, 50-59, 60-69, 70-79 and over 80 years. Statistical analysis was performed by the services of the Hematology and Cell Therapy and the services of Biostatistics of the 1st November E.H.U of Oran.

RESULTS

All the 15 hematological services of university hospitals participated in this study, only the Establissement Public Hospitalier Mascara and the Department of Epidemiology and Biostatistics of the 1st November E.H.U Oran. All centers reported their data; there was a 100% response to the survey.

A total of 1426 adult patients (≥16 years of age) were diagnosed with AML from 1 January 2006 through 31 December 2010 with a mean of 285.2 cases per year for the whole country, a mean of 19 cases per

Table 1. Clinical characteristics of patients (n=1426) at diagnosis.

	Median	Range
Age (years)	44.7	16-82
Male	41.1	
Female	44.6	
White blood cell count (10^9/L)	150	8.9-285.0
Hemoglobin (g/dL)	7.5	3-9
Platelets (10^9/L)	2.5	0.1-24.0

Figure 1. Distribution by French-British-American classification.

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hematology service per year and 95 cases for the 5 years of the study period. There was a very wide variation in the rate among the centers (2.2 to 34.2 cases /year) with a median of 24 cases/year.

Table 1 shows clinical characteristics of patients at diagnosis. The overall median age was 44.7 years (41 years for males and 45 for females), with a slight predominance of males. Clinical presentation of AML at diagnosis was most often characterized by severe anemia, thrombocytopenia, and leukocytosis up to 150.10^9/L. Of note was the presence of significant anemia in all of the patients (range of hemoglobin 3-9 g/dL). The distribution according to FAB classification showed a clear predominance of M2 type (36%), a low recruitment of M7 type (0.5%), while nearly 7% of cases were difficult to classify (**Figure 1**). Acute promyelocytic leukemia (APL) represented only 9.3%. **Figure 2** shows a trend of continuous annual increase in cases of AML where 246 cases had been registered in 2006, 265 in 2007, 292 in 2008, 303 in 2009 and 320 in 2010, with increase in the rate by 7.7%, 10.2%, 3.7% and 5.6%, respectively with a mean rate of increase of 6.8% for the whole study period. The crude annual incidence per 100 000 of the population continued to rise from 0.7 in 2006 to 0.9 in 2010 (**Figure 3**). The age-specific incidence varied from 0.41 for ages 16- 20 years, with a trend of a continuous increase in the rate, and a sharp increase to 2.65 after age 60 years reaching the highest 3.38 after age 80 (**Figure 4**).

According to their place of care, the patient distribution shows that over 70% had been diagnosed in the six oldest hematological centers in the country (**Figure 5**), while according to their place of residence, the city of Algiers had the highest frequency of 12.9% (**Figure 6**). Globally, 20% of AML were diagnosed in the whole western region of the country, 47% in the center and 33% in the east (**Figure 7**).

DISCUSSION

To our knowledge, this is the first report that registers the trends in incidence of AML in Algeria and compares incidence to that in Western countries. In this retrospective multicenter study, we identified 1426 cases of AML over a period of five years (2006-2010) with the collaboration of all of hematology services across the country.

The cytological features showed a predominance of elevated white blood cell count at presentation associated with severe anemia and thrombocytopenia, which may reflect a delay in presentation or delay in referral. Although this may be rooted in a possible higher tolerance of patients to disease manifestation
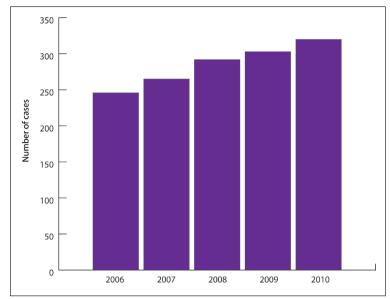

Figure 2. Annual number of acute myeloid leukemia cases.
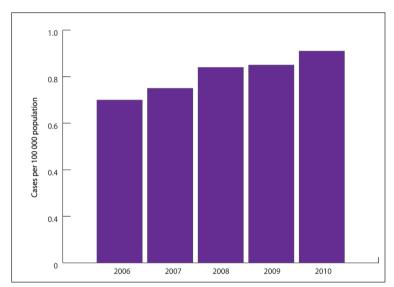

Figure 3. Annual incidence in cases per 100 000 population.

with subsequent delay in seeking medical advice, it may also implicate intricate difficulties in accessing the relevant health care system and/or limited awareness. Nonetheless, such a delay may detrimentally affect the overall outcome.[8]

The proportions of the FAB classification types are substantially the same as that described in the literature, but with a very low rate of M7 (0.5% versus 1.5%), and more indeterminate forms (7% versus 1%).[7] AML-M3 represented only <10% of all cases, which is less than expected when considering the relatively younger me-
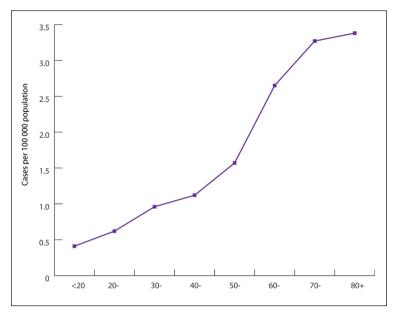
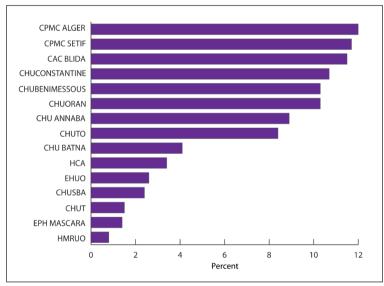**Figure 4.** Age-specific incidence in cases of acute myeloid leukemia.

Figure 5. Distribution of patients by center.

of the population census, but may be partly explained by an improvement in medical awareness, health care accessibility and recent expansion of health coverage. However, an actual increase of new cases related to the aging of the population and better diagnostics should also be considered.

The gross annual incidence per 100 000 people shows an increase from 0.7/100 000 in 2006 to 0.91/100 000 in 2010, resulting in 314 new cases per year in a population of 34.1 million people.[11] However, such a rate is still low compared to that of Western countries, which is 3/100 000 inhabitants in France.[12] In 2000–2003, the age-adjusted incidence rate of AML in the US was 3.7 per 100 000 for both sexes, 4.6 per 100 000 for males and 3.0 per 100 000 for females.[13] Further improvement in early diagnosis, early referral and collaborative work between primary care hospitals and the private sector of the health care system with tertiary care hematology centers should help in improving the rate of capturing such cases and proper referral for optimal management.

As expected, AML cases were clustered more during later adulthood as seen universally. The annual incidence shows increasing age-specific rates from 0.41/100 000 inhabitants before the age of 20 years to over six times the value (2.65/100 000 inhabitants) after 60 years and more than eight times the value (3.38/100 000 inhabitants) after 80 years. Such a trend has also been shown universally. The distribution of the proportion of prevalent cases of all leukemias in the UK showed that 42.8% of patients are age >65 years with a median age of 65 years.[14] From 2000 to 2003, the US incidence rate in people aged <65 years was only 1.8 per 100 000 persons, whereas the incidence rate in people aged over 65 years was 17 per 100 000 persons.[15] The relatively younger median age at diagnosis of AML in Algeria may reflect the relatively younger population in comparison to the West.

Of note, there is a much younger age at presentation in Algeria, with an overall median age of 45 years versus 63 years in Europe[14] and USA.[15] This young age is found both in men (median age, 41 years) than in women (median age, 45 years) and is explained by the character of the young population of Algeria where more than half of Algerians are under 30 years.[16] Being young makes a large proportion of our patients eligible for curative intent with the plan of management including hematopoietic stem cell transplant (HSCT). This may necessitate a change in practices to incorporate such a modality in the therapeutic package and should call for collaborative research trials for high-risk patients who are not eligible for such

dian age of our patient population (45 years). Such a phenomenon may be related to ethnic factors or to the natural history of APL which can present with a very acute course that should either be treated swiftly or patients die before they reach a tertiary care facility.[9] The marginal male predominance with a sex ratio of 1.16 matches distributions in most countries.[10]

There was a clear trend of a steady increase in the annual frequency of AML during the study period which cannot be explainable by the expected yearly rise

a procedure.

The distribution of patients in view of their place of care and of stay shows that the hematology department of CPMC (the first and oldest hematology department in the country) is leading the recruitment of patients in Algiers, the capital city of Algeria, which is located on the Mediterranean Sea coast and may reflect the population density. The wide variation in recruiting patients between centers can be used in the future to allow center-to-center transfer of patients in case of capacity overflow. In addition, training programs to advance hematology subspecialties can be tailored and assigned to those centers with a larger patient load. The study also highlights the difference in distribution of patients in relation to demographics in the different regions of the country. The epidemiological data identified the order of AML among other hematologic malignancies,[17] occupying the top spot with acute lymphoblastic leukemia and highlights important parameters like the annual incidence and the distribution of patients by health regions of the country. Such data helps organize the prioritization of existing resources, assess the needs, and calculate and planned expenditures on health infrastructure, especially construction of new units for HSCT, and improves means of comprehensive diagnostics and treatment. The development of HSCT, which was initiated in 1995 in Algiers, represents a great advancement in AML care. Algeria currently has two large HSCT units, CPMC Algiers, which can perform 120 allografts per year[18,19] and a second one that opened in May 2009 that serves those who need autologous transplants[20,21] and hopefully will expand to add allografts in the near future. In 2008-2009, 195 HSCT were reported from Algeria to the Eastern Mediterranean Bone Marrow Transplant (EMBMT) group and 64 (32.8%) were performed for AML (56 in first complete remission and 8 in second remission) making AML the most common single indication for allogeneic HSCT in Algeria.[22] However, this number represents only a small minority (<10%) of all AML cases registered in our current report for the same period 2008-2009 (total, 595). Because a much higher proportion of AML patients might need an allogeneic HSCT due to associated high-risk features, the current situation creates a significant gap between the number of AML who are potential candidates for allogeneic HSCT and the actual number of AML patients receiving a transplant and should be considered in future planning to optimize patient outcome. HLA identical sibling donors may reach 70% in Algeria, making allogeneic sibling transplant the preferred modality in such an aggressive disease when indicated.[23] From
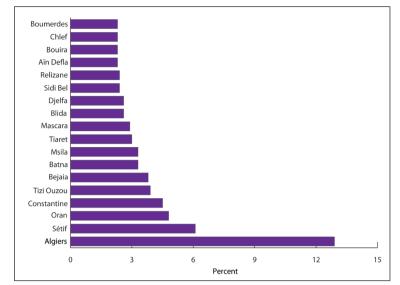

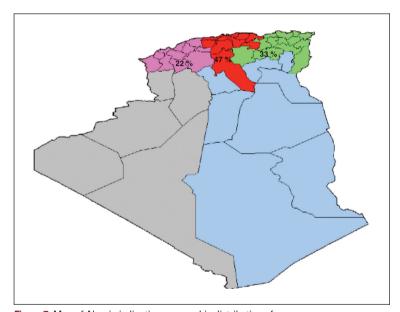**Figure 6.** Distribution by city.

Figure 7. Map of Algeria indicating geographic distribution of cases.

another perspective, this epidemiological study has allowed us to show the very young character of our patients and indicates the need for serious thought to better adapt new therapeutic strategies, particularly those used in children, which would be different from those used in Europe or the US.[24]

The Algerian Group for the Study of AML and myelodysplasia has been established to develop protocols for consensus in the diagnosis and management of hematologic malignancies, including AML. Further data collection related to the cytogenetic and molecular back-

ground as well as treatment and outcome would greatly help in understanding this aggressive disease and refine long-term strategies to improve outcome.

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