

# Descriptive and Analytical Study of Acute Leukemia in Adults in Eastern Algeria

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**Abstract-** Acute leukemia (AL) is a group of malignant hemopathies characterized by monoclonal intramedullary proliferation of abnormal hematopoietic cells, the maturation process of which is blocked at the "Blast" stage. In these pathologies, an abnormal cell clone proliferates. By its character of anarchy, of nonresponse to normal regulators of cell proliferation, and its invasive character, this clone assumes all the characters of malignancy. The diagnosis of ALL can no longer be based solely on morphological and cytochemical characteristics but must include the elements of the immunological phenotype of leukemic cells. Currently, a classification based on immunophenotypic and cytogenetic data, as well as on molecular biology data, is necessary for the determination of the optimal treatment. The objective of this work is to reach a descriptive approach of acute leukemia in the region of Annaba, in the east of Algeria. Description of the epidemiological, clinical, and cytological characteristics of the cases of acute leukemia collected in the Hematology Laboratory of Dorban Hospital over a period of 6 years. Analysis of the results of our study and their comparison with those published in the literature, with a reminder of the epidemiological and diagnostic data. The retrospective study was conducted in the division of the hematology hospital of Sidi Ammar-Annaba, during the period from January 2018 to July 2019. This study was based on data from 50 patients. During our study period, the results show that 50 cases of acute leukemia confirmed by the myelogram were notified. The annual average is 12.3 cases. The collected data were made in Annaba at the CHU-Dorban. We noted a variety of clinical signs and a variety of symptoms represented mainly by fever (100%), anemia (100%), hemorrhagic syndromes (30, 6%), and splenomegaly (80.6%), for the myelogram. Acute lymphoblastic leukemia (ALL) was predominant with 25 cases. In conclusion, we can say that. Acute leukemia in adults in eastern Algeria can be expressed by a variety of symptoms and hematological disorders, in addition to a series of associated conditions.

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## Introduction

Among the malignant hemopathies defined by an intra-medullary monoclonal proliferation of abnormal hematopoietic cells with a maturation process blocked at the "Blast" stage, we note acute leukemias (LA).

The main consequence of this proliferation is the accumulation of these blasts in the marrow, in the blood, and possibly in other organs. In addition, there is a deficit in the production of mature cells, hence the

installation of a table of spinal insufficiency associating febrile neutropenia, anemic syndrome, and hemorrhagic syndrome and their clinical consequences (1,2), thus requiring a rapid and precise diagnosis to establish an appropriate therapeutic approach (3). Depending on the origin of the precursor involved, we distinguish:

Acute lymphoblastic leukemia (ALL) is especially observed in children (4), but also in adults after 50-60 years.

Acute Myeloid leukemia (AML), the frequency of

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which increases with age (median around 63 years) (5).

Exceptionally, the malignant cells can express the markers of the two lines; these are acute biphenotypic leukemias (6,7,8).

The Franco-American-British classification "FAB" is based on the examination of stained slides and the use of cytochemical reactions, and which has made it possible to dissociate myeloid leukemias from non-myeloid "lymphoblastic" leukemias (9,10,11)

The biological work carried out on acute leukemias, in particular in molecular genetics, has made it possible in recent years to make significant progress in understanding leukemogenesis (12,13,14)

The diagnosis and prognosis are based on the morphological examination of blasts, blood cells, and bone marrow, as well as immunophenotyping and cytogenetic and molecular study.

If treatment is the responsibility of specialized centers (based on chemotherapy, sometimes associated with hematopoietic stem cell transplantation), the role of the biologist is essential, in particular for diagnosis, monitoring during treatment, and then monitoring after remission (15).

In the early 1990s, adult acute lymphoblastic leukemia (ALL) had a very poor prognosis with long survival rates in less than 10% of cases. Recent advances in the biological field of ALL have led to a better understanding and a new classification of the disease.

The diagnosis of ALL can no longer be based solely on morphological and cytochemical characteristics but must include the elements of the immunological phenotype of leukemic cells. Currently, a classification based on immunophenotypic and cytogenetic data, as well as on molecular biology data, is necessary for the determination of the optimal treatment.

Over the past thirty years, therapeutic strategies used in adults have followed the evolution of childhood ALL treatments. However, their results remain much lower than those observed in children. As in children, therapeutic strategies taking into account the aggressiveness of the disease are now applied to adult ALL.

Generally, the initial diagnosis of acute lymphoblastic leukemia is based on the findings of cytomorphological studies of peripheral blood and bone marrow. The World Health Organization requires a blast percentage of at least 20% in the bone marrow or peripheral blood smear for the diagnosis of ALL. However, one study found cases with the unexpected presence of blasts in the fluid cerebrospinal (CSF), but

not in peripheral blood. These cases illustrate that meningeal involvement can occur as the first sign of ALL and can develop even in the absence of systemic disease.

## Materials and Methods

### Study area

The study was carried out in the Department of Biochemistry and Cellular, and Molecular Biology of the University Mentouri Constantine (East of Algeria) in coordination with the care unit of Sidi Ammar and the Dorban hospital specialized in hematology of the city of Annaba (East of Algeria).

(EPS), Sidi Ammar from the city of Annaba and the Dorban hospital specializing in hematology in the same city of Annaba has an enabling environment (human and material endowment) to carry out this study. The city of Annaba is located in the far east of Algeria, on the Mediterranean coast near the Tunisian borders. With an average annual temperature of 27.3° C, Sokoto is, on the whole, a coastal area, the maximum temperatures for most of the year are generally below 40° C. The rainy season extends from September to the month of May, during which the showers are almost daily.

### Study population

Our study involved 50 cases of acute leukemia, collected in the Department of Hematology at Dorban Hospital in the city of Annaba. Our work is based on the study of the files of these 65 patients with this pathology, men, and women combined.

### Type and period of study

This is a descriptive and analytical retrospective study of 50 cases of patients diagnosed with acute leukemia between January 2018 to July 2019.

### Data collection

We used the clinical and biological information sheets sent with the myelograms and hemograms to the Hematology Laboratory at Dorban Hospital in Annaba and the laboratory registers.

These files served as the basis for the exploitation of their data in a pre-established file (appendix), which made it possible to gather and analyze the main epidemiological, clinical, and biological characters identified. This sheet contains the following items:

- Biological data,
- Epidemiological data,
- Clinical data.

### Inclusion criteria

In our work, we included patients of both sexes, with acute leukemia confirmed by myelograms.

### Exclusion criteria

The other forms of leukemia were excluded from our study.

### Data entry and analysis

Data were collected from files of patients with LA at the Hematology Laboratory at Dorban Hospital. We thus filled out the patient files, which were then entered and computerized on Microsoft Excel 2007 software and SPSS version 20 for Windows was used for descriptive statistics. Results were calculated as frequencies (%), means, and standard deviations (SD).

We used the *Chi*-square test to study correlations between histology grade and serological tests, respectively, different manifestations of the disease, in addition to the correlation between age and histology grade, respectively comorbidities. The statistical significance was  $P < 0.05$ .

### Limits of our study

Lack of certain important information in the records, such as imprecise history, did not allow us to know some etiological factors.

## Results

### Epidemiological aspects

#### Age distribution

Eight patients were between 18 and 20 years of age or 16% of adults. Twenty-six patients were between 21 and 59 years old, or 52% of adults, with a peak of 52 (6 patients).

Ten patients were between 60 and 75-year-old, or 20% of adults. Six patients were over 75 years of age, 12% of adults (Figure 1).

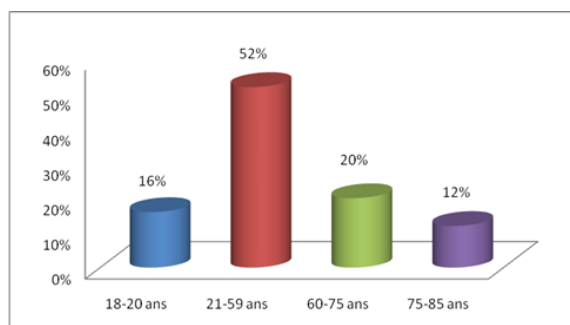


Figure 1. Distribution of patients by age group

### Gender breakdown

The population analyzed showed a male predominance for all cases of LA. While 33 patients were male or 66%, and 17 were female or 34% of the workforce with a sex ratio of 1.94.

### Clinical and paraclinical aspects

In this study, we searched for all clinical and paraclinical morphological signs or manifestations, as well as any pathology associated with leukemia (Figure 2). For a reason for consultation, the main symptoms were dominated by fever (100%) and hemorrhagic syndromes (30.6%) (Figure 3). The clinical images found are dominated by the anemia that is represented in all our patients, followed splenomegaly with 80.6% (Figure 2). The paraclinical manifestations are revealed by the data of the hemogram and the myelogram.

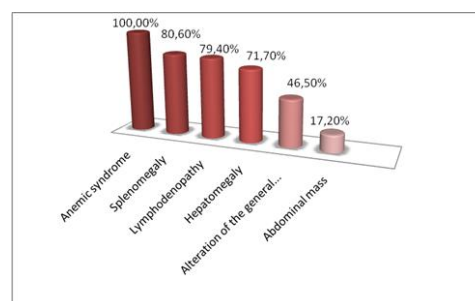


Figure 2. Distribution of patients by paraclinical signs at the entry

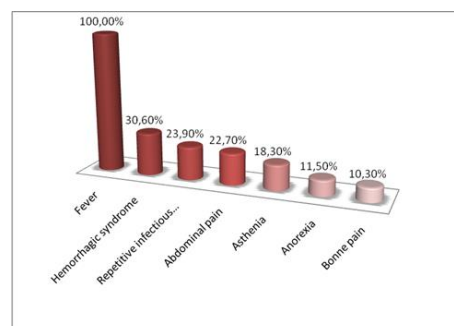


Figure 3. Breakdown of 22 patients by reason of consultation

For biological tests, We observed two cases for which LA was discovered on a follow-up assessment. A case of a 34-year-old patient undergoing treatment for pleural tuberculosis who had polynucleiosis with neutrophils and a blast alarm. Another case of a 22-year-old patient followed for untaged chronic refractory anemia since the age of 10.

On the other hand for hemathological test, the hemogram shows that Hemoglobin varied between 2.8 g/dl and 12.9 g/dl with a median of 6.6 g/dl and an average of 7.9 g/dl. 5 adults had an Hb  $< 5$  g/dl, or 10%

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of the cases in total. 12 adults had an Hb between 5 and 7 g/dl, or 24% of the cases. Another 28 patients had an Hb between 7 and 10 g/dl, or 56% of the cases, and 5 patients had an Hb > 10 g/dl, for a total of 10% of the cases.

We noted that the results of the VGM varied between 57 and 119 fl. The MCT varied between 14 and 37 pg. And the reticulocytes were between 5,100 and 32,000/mm<sup>3</sup>.

Thus 11 patients had an artery-induced microcytic hypochromic anemia (22% of the cases). And 39 adults had normocytic areregenerative anemia (78% of cases).

The number of GB varied between 870 and 260,000 elements/mm<sup>3</sup>. Ten adults had leukopenia (20% of cases).

10 other adults had GB between 4000 <GB <10,000 elements / mm<sup>3</sup> (20% of cases).

Twenty-one patients had leukocytosis with GB between 10 000 and 50 000 elements / mm<sup>3</sup> (that is 42% of the cases). Five patients had a major leukocytosis with GB > 50,000 elements / mm<sup>3</sup> or 10% of the cases) (Figure 4).

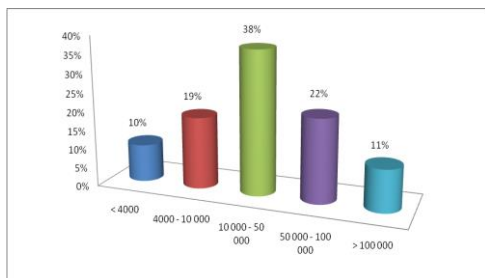


Figure 4. Patient distribution according to leukocyte counts

The number of platelets ranged from 6,000 to 271,000 elements/mm<sup>3</sup>. 17 patients had major thrombocytopenia with platelets <30,000 elements/mm<sup>3</sup> (34% of cases). 9 others had platelets between 30,000 and 50,000/mm<sup>3</sup> (18% of cases). 16 adults had platelets between 50,000 and 150,000 elements/mm<sup>3</sup> (or 32% of cases). 8 patients had platelets > 150,000 elements/mm<sup>3</sup> (16% of cases) (Figure 5).

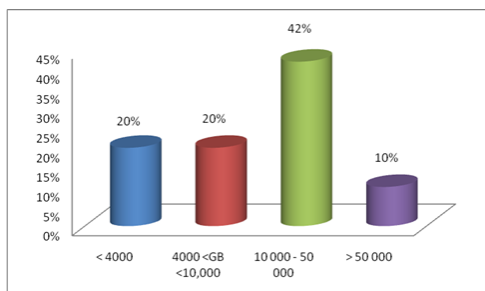


Figure 5. Breakdown of patients by platelet count

The results of the Myelogram show that the rate of spinal cord blasts varied between 30% and 96%, with an average of 75%. In the majority of patients, the blast rates varied between 25% and 90%, with an average of 63%. The blast rate for ALL was 82% compared to 61% for LAM (Figure 6). For DFO Cytochemistry, It was performed on all of the spinal smears in our series. The reaction was positive in 32 cases, or 53% of the cases, while in 47%, the MPO was negative, making a total of 28 cases, of which 16 were acute lymphoblastic leukemias.

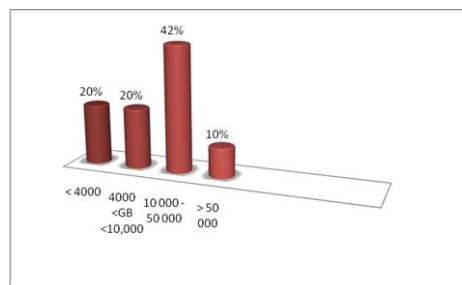


Figure 6. Distribution of patients according to the results of the myelogram

## Discussion

Medical literature reports that LA is the leading cause of cancer in Europe and the United States (12). In adults, ALL is four times less common than LAM (approximately 5% of leukemias) (5).

In our series, the distribution according to age showed an impairment of all age groups, with an average age of 33.2 years and extremes ranging from 22 to 83 years. In a study published in 2009 by the regional register of malignant hemopathies of Basse-Normandie in France over a period of 8 years (1997-2004), the average age for ALL was 25 years compared to 63 years for LAM (13).

In 2011, a retrospective study carried out at the hematology laboratory of the CHU Ibn Rochd in Casablanca over a period of 4 years (2004-2007), reported an average age of 38 years for LAM and 21 years for LAL (14).

At the MedVI CHU in Marrakech, a study of 378 cases of LA reported an average age of 35.3 years for LAM and 13.8 years for LAL (15).

In Brazil, the study by Rego *et al.*, in the state of Piauí, between 1989 and 2000, reported an average of 9 years for LAL against 34 years for LAM (16).

Our results are similar to those of the Casablanca University Hospital, the Marrakech University Hospital, and the Brazilian series, but are below average in Lower

Normandy, Europe (17), and also in the United States (18).

LAMs are rather pathologies of the elderly subject with an average age of 63 years and a very marked increase in the incidence from 60 years (4). Age > 60 is a poor prognosis. In our series, 32% of adults were over the age of 60 (11).

In our series, there is a male predominance with a sex ratio M/F all ages combined at 1.94, which is consistent with the previous report showed sex is a prognostic factor (19).

We carried out a comparison of the sex ratio with a study carried out between 1998 and 2002 at the Farhat-Hached hospital in Sousse in Tunisia and which dealt with 193 cases (20), as well as with two other studies carried out at the Ravoahangy hospital. Andrianavalona Antananarivo in Madagascar between January 2013 and December 2014 (21), and at the Valence Hospital Center (CHV) in the Drôme department in France between 2005 and 2010 (22).

The distribution of cases according to their sex was comparable to that of the different series and confirmed the male predominance also found in the literature (5,12).

Indeed, in Europe (17), the incidence rates of acute leukemia, to a lesser extent for ALL, are higher in men than in women, with a sex ratio of 1.2.

In the United States, this difference between the sexes is much more pronounced among whites (70% more leukemia in men and 60% more in women) than in blacks (30% and 15%, respectively) (12).

In Morocco, among 814 cases of diagnosed LA, 64% of AML cases had a sex ratio M/F of 1.2, and 30% of ALL with a sex ratio M/F of 1.05. The male predominance is also found in the series of the CHU of Marrakech and in Basse-Normandie as well as in the other series of the literature that we consulted.

For the clinical signs and, more specifically, the anemic syndrome, which is a subjective syndrome more or less appreciated depending on the case. In our series, 90% of the cases presented an anemic syndrome at diagnosis; in the series of Sintha *et al.*, 71% of the patients presented an anemic syndrome (23).

For hemorrhagic syndrome, It was present in 48% of cases in our series and has always been associated with one or two other signs of spinal cord syndrome.

In a study carried out at the Tunisian center between 1998 and 2008 and involving 281 patients, 15% of patients had a hemorrhagic syndrome (24), while it was present in 21% of the cases in a study carried out by Sintha *et al.*, in India (25).

The infectious syndrome which was specially described by fever as the most frequent clinical presentation at diagnosis (3). It can be of varying intensity. In our series, the infectious syndrome was present in 45% of the cases. In the Rego *et al.* series in Brazil (16), 58% of patients had an infectious syndrome at diagnosis, while Sintha *et al.*, in India reported a higher frequency of around 80%.

Blood count show in our series that the majority of our patients were anemic, and all had hemoglobin less than or equal to 10 g/dl, of which 15% had very deep anemia (less than 5 g/dl). All of our patients had regenerative anemia. It was normochromic normocytic in 87% of the cases.

White blood cells were greater than 100,000 / mm<sup>3</sup> in 7%; this frequency is comparable to those reported in the series of Sintha *et al.*, in India (8.3%) (25), and in the Tunisian series (14%) (20).

We noted severe thrombocytopenia with a risk of a cerebral hemorrhage in 33% of the cases. This frequency is comparable to that reported by Jmili *et al.*, in Tunisia (35%) (20), while in the Sintha *et al.*, series only 11.7% of patients had severe thrombocytopenia (25).

For the Myelogram and the rate of spinal cord blasts. In our series, the average spinal cord blast was higher in children (88%) than in adults (63%). Usually, the rate of spinal blasts is greater than 90% in ALL (25); in our series, the average of blasts for ALL was 82%.

The fastest and most informative cytochemical reaction is that of myeloperoxidase. Its positivity ( $\geq 3\%$  of blasts with reactivity) eliminates or confirms the myeloid origin of the blasts (10).

This staining is, therefore, particularly useful and makes it possible to distinguish an unripened or with minimal maturing myeloblastic leukemia from acute lymphoblastic leukemia. However, in 7 cases of our series, the MPO was negative with the difficulty of classification of the LA in the absence of morphological characteristics specific to a variety or another, hence the interest to resort to other explorations (Immunophenotyping and cytogenetics) to determine the line of belonging.

Acute leukemia is a heterogeneous composition of diseases whose initial features and course are very different from one group to another.

Meticulous clinical examinations most often allow the diagnosis of acute leukemia to be suspected, which will then be confirmed or refuted by more specific additional examinations.

Biological examinations currently occupy a fundamental place in the establishment of the diagnosis

and make it possible to adapt the treatment to the foreseeable severity of the disease.

Immunological, cytogenetic, and molecular techniques must complement those existing for better management of LA in our context.

This work made it possible to record a certain number of points:

Raising awareness among healthcare professionals (general practitioners and specialists) as well as raising awareness on a larger scale of the general population can reduce treatment times and indirectly improve the prognosis of these pathologies and the daily lives of patients.

The need to create and develop a national cancer registry. This tool would make it possible to know precisely the share that belongs to each pathology, its evolution, and variations over time, and would help in the development of diagnostic and management protocols.

The need to develop flow cytometry units and the means of cytogenetics and molecular biology studies for optimal diagnostic, prognostic, and therapeutic treatment.

### **Limits and perspectives**

In our study, the difficulties consisted of the presence of blasts without morphological signs of differentiation, making it possible to classify them. Indeed, the interest of the new techniques used in acute leukemias in particular cytogenetics, immunophenotyping, and molecular biology is well established and currently enter into the criteria of diagnostic and prognostic classification of LA and, in particular, in the evaluation of residual disease

In recent years, several research projects concerning acute leukemia have been launched. These projects are intended to study the cytogenetic and molecular alterations that cause different types of acute leukemia. One of the aspects analyzed is the blocking of cell differentiation from hematopoietic stem cells, which is the culmination of the process of leukemogenesis and the major cause of the manifestation of the disease.

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