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Acute Leukemia in Niger: Epidemiological, Diagnostic and Therapeutic Aspects

Amadou Djibrilla-Almoustapha[1,2*], Badé Malam-Abdou[1,2], Abdourahamane Yacouba[2,3,4], Moussa Souley[1], Moustapha Maman Brah[3], Moustapha Elhadji-Chefou[5], Boubacar Marou-Soumana[2,6], Samaila Aboubacar[2], Ousseini Fanta[2], Maman Rabiou Badé[1], Oumarou Adamou-Chaibou[1]

[1]Department of Hematology-Oncology, National Hospital of Niamey, Niamey, Niger
[2]Faculty of Health Sciences, University of Abdou Moumouni, Niamey, Niger
[3]Department of Medicine, Zinder Hospital Regional, Niger
[4]Departtment of Biology, Amirou Boubacar Diallo National Hospital, Niamey, Niger
[5]Faculty of Health Sciences, University of Dan Dicko Dankouloudo of Maradi, Maradi, Niger
[6]Laboratory of Biology, National Hospital of Niamey, Niamey, Niger
Email: *amdjibrilla@gmail.com

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Abstract

Objective: Improve the care of patients followed for acute leukemia in the Oncohematology department of the National Hospital of Niamey. **Methods:** This was a prospective study, over a period of 2 years from January 1, 2018 to December 31, 2019, in patients with acute leukemia in the Oncohematology department of the National Hospital of Niamey (HNN), whose diagnosis was made on a blood smear associated with a myelogram and immunophenotyping and who were consenting. **Results:** We collected 25 cases of acute leukemia confirmed by myelogram and immunophenotyping. The mean age of the patients was 31.32 years, with a predominance of women, a sex ratio of 0.92. Pupils and students were in the majority with 40% and most came from the Niamey region, *i.e.* 68%. Anemic syndrome was the most common clinical sign in 96%. ALL predominated in 64% of cases. On the blood count, the hyperleukocytosis was more marked in AML (mean white count: 197256.6 elts/mm^3) than in ALL (137891.6 elts/mm^3), it was the same for thrombocytopenia which is more marked in AML (75588.89/mm^3) than in ALL (52156.25/mm^3). Therapeutically, 52% of patients received chemotherapy. The mean overall survival was 16.223 ± 3.191 months, including a mean survival for AML of 6.853 ± 1200 months compared to 21.720 ± 5.920 months for ALL. **Conclusion:** Acute leukemia still remains a major problem in our context, due to the precariousness of limited financial, diagnostic and therapeutic resources. Thus reflecting in our results, the increasing number of cases, the diagnostic delay and the guarded prognosis. This is the reality in several other

countries in the sub-region and even in certain developed countries.

Keywords

Acute Leukemia, ALL, AML, Hematology-Niamey National Hospital (HNN), Niger

1. Introduction

Acute leukemias (AL) are hematologic malignancies characterized by clonal proliferation of hematopoietic stem cells with blocked maturation invading the bone marrow and hindering the production of normal blood cell lines. Thus, it results in bone marrow failure [1]. According to WHO data released in 2020, the incidence of all leukemia is 474,519 new cases, including 311,594 deaths [2] [3]. There is Acute Myeloid Leukemia (AML), more common in adults in 80% of cases, with an incidence of 2.5/100,000 and increases with age up to 12 - 13/100,000 in people over 65 years old. Acute Lymphoid Leukemia (ALL) is proportionally more common in children [1]. However, biological work, particularly in molecular genetics, has enabled notable advances in recent years. Treatment is based on chemotherapy, sometimes combined with hematopoietic stem cell transplantation. Practitioners from black Africa, often faced with a lack of technical support, face certain death in the event of acute leukemia [4] [5]. In Niger, as in other African countries, acute leukemia is considered a scourge of real magnitude, labeled with certain death [4]. Very few studies have focused on this aspect in our department, hence the aim to study the epidemiological, diagnostic and therapeutic aspects of acute leukemia in the Hematology department of the Niamey National Hospital.

2. Methods

2.1. Study Type and Period

This was a prospective descriptive and analytical study conducted at the National Hospital of Niamey in the Oncology-Hematology department, spanning from January 1, 2018, to December 31, 2019, for a duration of 2 years.

2.2. Inclusion Criteria

All patients being treated for Acute Leukemias, regardless of age or gender, who had blood smears, bone marrow examinations, and immunophenotyping used to confirm the diagnosis of acute leukemia and who agreed to participate fully in study.

2.3. Diagnostic and Therapeutic Method

The diagnosis of AL was made based on strong clinical suspicion or abnormalities in the blood count. Our diagnoses were confirmed by cytology (blood smear and bone marrow examination) interpreted by two Oncology-Hematologists at the Oncology-Hematology department of the HNN, and further confirmed by

immunophenotyping at the CERBA laboratory (France). The patients were responsible for the extension assessments, including cerebrospinal fluid cytology, chest X-rays, abdominal ultrasounds, laboratory tests, and pre-therapeutic assessments, which is why some patients were unable to complete these assessments. The diagnostic and therapeutic management was financially the responsibility of the patients regardless of the number of treatments. It is within these contexts that the results of our study were derived. We used the MARALL protocol (Morocco-Acute Lymphoblastic Leukemia) for Acute Lymphoblastic Leukemias and the AML 99 Protocol for AML.

2.4. Statistical Analysis

The collected information included: age, sex, sociodemographic data, clinical manifestations, and diagnostic and therapeutic methods. Data analysis was performed using Excel 2013 and R software version 3.5.3. For categorical variables, the Chi-square test was used to calculate the p-value. For continuous variables, the Student's t-test was conducted to calculate the p-value. The Kaplan-Meir test was performed to determine the survival of patients with acute leukemia. The threshold for statistical significance was set at $p < 0.05$.

2.5. Study Limitation

The extremely low socioeconomic status of the patients and their families resulted in some crucial diagnostic tests not being completed (including karyotype in all patients and FISH) and the unavailability of certain treatment medications (including marrow transplant).

3. Results

3.1. Sociodemographic Characteristics

Over a period of two years, 25 cases of acute leukemia (16 cases of ALL and 9 cases of AML) confirmed by myelogram associated with immunophenotyping were diagnosed in the Hematology department of the National Hospital of Niamey, *i.e.* an annual frequency of 12.5 (8/year for ALL and 4.5/year for AML).

Female patients, *i.e.* 52.00% (n = 13), were in the majority, sex ratio = 0.9. Thus, those under the age of 18 were the most represented, *i.e.* 36% (n = 9) of cases, the average of which was 31.32 ± 19.63 years with extremes ranging from 5 to 71 years. The personal history was dominated by infections, *i.e.* 52.00% (n = 13) of cases, 20.00% (n = 5) had a notion of exposure to toxic substances.

3.2. Clinical Features

Anemic syndrome was the most frequent clinical sign, *i.e.* 96% (n = 24), followed by infectious syndrome in 88% (n = 22), and tumor syndrome in 84% (n = 21). On the other hand, hyperleukocytosis was the most frequent reason for consultation, *i.e.* 45.83% (n = 11) of cases (for reference purposes), followed by splenomegaly and lymphadenopathy in 20.83% (n = 5) and 16.67 respectively. 16.67%

(n = 4) of cases.

3.3. Diagnostic Characteristics

3.3.1. Types of Leukemia (Figure 1)

ALL was predominant in 64% (n = 16) of cases, while AML accounted for 36% (n = 9), including 34% for AML0 (n = 3), 11% for AML1 (n = 1), 22% for AML2 (n: 2), 11% for AML3 (n = 1), 11% for AML4 (n = 1), and 11% for AML5 (n = 1).

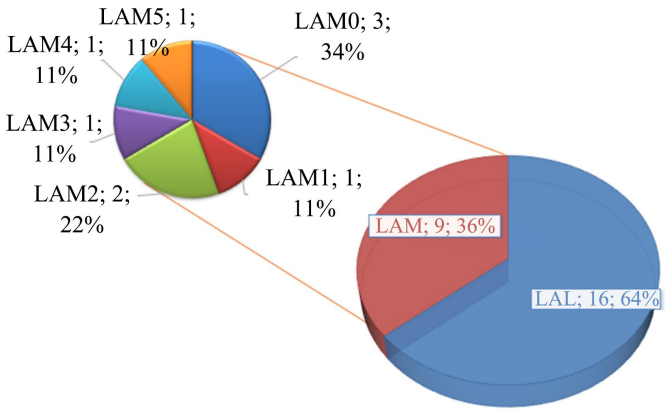

Figure 1. Distribution of patients according to type of acute leukemia.

3.3.2. Types of Acute Leukemias and Hematological Parameters

The average white blood cell count for patients with AML was 197256.6 cells/mm^3 compared to 137891.6 cells/mm^3 for patients with ALL. There was no statistically significant difference (p = 0.73).

The average hemoglobin level for patients with AML was 7.11 g/dL compared to 6.28 g/dL for patients with ALL. There was no statistically significant difference (p = 0.47).

The average platelet count for patients with AML was 75588.89/mm^3 compared to 52156.25/mm^3 for patients with ALL. There was no statistically significant difference (p = 0.15) between the two groups.

3.3.3. Types of Acute Leukemias and Reticulocyte Count

The average reticulocyte count for patients with AML was 87333.33/mm^3 compared to 60906.25/mm^3 for patients with ALL. There was no statistically significant difference (p = 0.15). (**Figure 2**)

3.4. Patient Survival According to Type of Acute Leukemia (Figure 3)

Out of the 25 diagnosed patients, 52% (n = 13), including 69.3% (n = 9) with ALL and 30.7% (n = 4) with AML, received chemotherapy treatment and benefitted from the MARALL protocol for ALL and the AML 99 protocol for AML. After the induction phase, 73% of ALL patients and 37% of AML patients achieved complete remission. Patients with AML (average 6.853 ± 1.200 months) had lower survival rates compared to patients with ALL (average 21.720 ± 5.920 months).

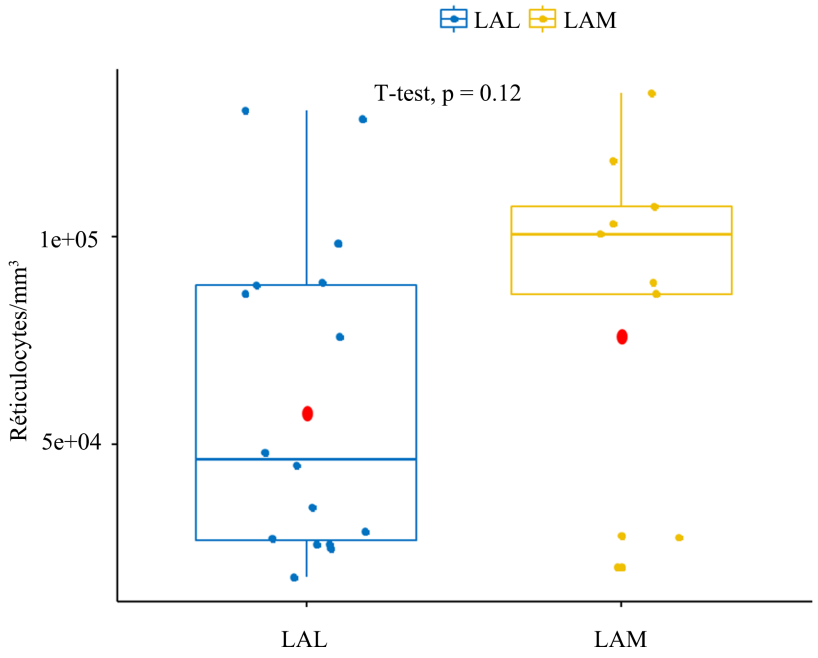

Figure 2. Distribution of types of acute leukemias based on reticulocyte count.

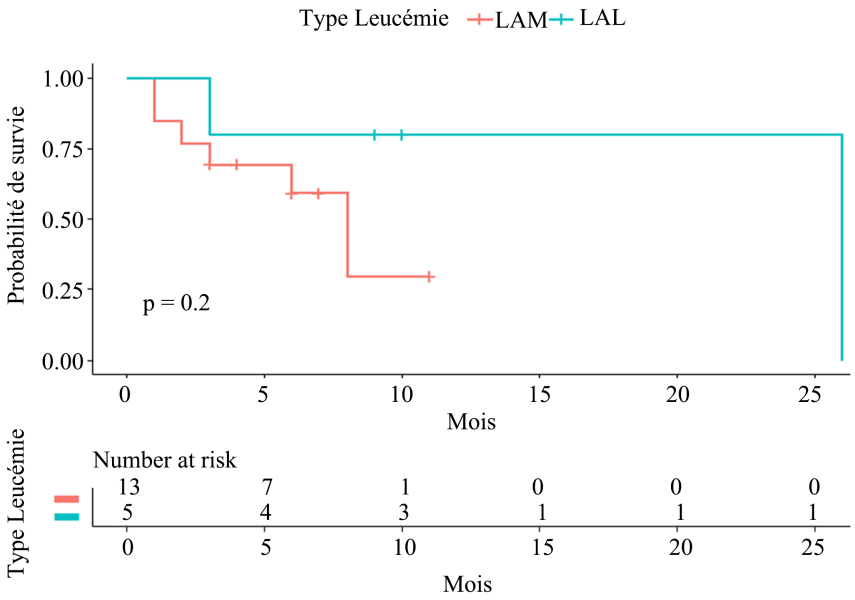

Figure 3. Median survival of patients followed.

4. Discussion

4.1. Sociodemographic Characteristics

The annual frequency of acute leukemias during our study was 12.5 per year (8 per year for ALL and 4.5 per year for AML. Ngolet L, in Congo in 2022, Ouédraogo RC at the YO University Hospital in Ouagadougou in 2008, as well as Mbensa L. *et al.* in Mali in 2018 reported frequencies lower than ours, at 1.9 per year, 4.5 per year, and 4 per year respectively [6]-[8]. The average age of our patients was 31

years, ranging from 5 to 71 years old. The age group of 0 to 18 years old was the most represented (36%). According to literature, the distribution of acute leukemias by age varies depending on the type of leukemia. In ALL, a first peak is observed between 2 and 4 years old, followed by a decrease during childhood, adolescence, and young adulthood, and then a second peak between 25 and 50 years old [1]. For AML, the median age of diagnosis is 70 years [9]. The majority of our patients were students, accounting for 40% of cases. This situation is commonly described by some authors in Africa [8]. In our series, we found a history of recurrent infections in 52% of cases and exposure to toxic substances in 20% of cases. Although not specific to leukemia, these situations have been reported in the literature, such as the risk of exposure to ionizing radiation, whether accidental exposure during natural disasters or in the case of occupational exposure [1].

4.2. Clinical and Paraclinical Characteristics

Anemic syndrome was found in 96% of cases, infectious syndrome in 88% of cases, and tumoral syndromes such as splenomegaly and lymphadenopathy in 20.83% and 16.67% of cases, respectively. Hemorrhagic syndrome and bone pain were each present in 4.17% of cases. This situation, commonly observed in series related to acute leukemias, characterizes a blockage of marrow maturation leading to marrow failure, clinically manifested by anemia, hemorrhagic syndrome, infectious syndrome, and in some cases, tumoral syndrome to varying degrees [6] [8] [10].

4.3. Paraclinical Aspects

4.3.1. Type of Acute Leukemia

Twenty-five (25) cases of acute leukemias were diagnosed, with 15 cases (64%) being ALL and 9 cases (36%) being AML. Ngolet L, in Congo in 2022, Ouedraogo RC at the YO University Hospital in Ouagadougou, and Mounkaila B. *et al.* in Niger reported 68.2%, 80%, 80% of ALL cases and 31.8%, 20%, and 20% of AML cases respectively [7] [11] [12]. Among the AML cases in our study, representing 36% (n = 9), subtypes included 34% AML0 (n: 3), 11% AML1 (n: 1), 22% AML2 (n: 2), 11% AML3 (n: 1), 11% AML4 (n: 1), and 11% AML5 (n: 1). According to the literature, the classification of AML into different types, with recognized clinical correlations, initially relied on morphological criteria (FAB). The identification of specific genetic abnormalities in certain types of leukemias, both acute and "non-acute" (myelodysplastic syndrome (MDS)), has led to new proposals from the WHO, which categorizes cases as 5% AML0, 10% AML1, 30% - 40% AML2, 15% - 25% AML3, and 8% - 15% AML5 [11] [13] [14].

4.3.2. Type of Acute Leukemia and Hematological Parameters

1) White Blood Cell Count

In our series, the average white blood cell count was 197256.6/mm^3 for AML and 137891.6/mm^3 for ALL. This confirms the leukocytosis observed in African

series as well. Hyperleukocytosis is a poor prognostic factor whether it is in AML or ALL, once it exceeds 50,000 cells/mm^3 [4] [7]

2) Hemoglobin

The average hemoglobin level in our series was 7.11 g/dl for AML and 6.28 g/dl for ALL. This confirms the anemic syndrome described in nearly all of our patients (96%). Literature data reports anemia in almost all cases of acute leukemias, a result of marrow failure due to maturation blockage of the myeloid lineage, leading to a deficiency in the production of red blood cells needed by the body [15].

3) Platelets

In our series, the average platelet count was 75588.89/mm^3 for AML and 52156.25/mm^3 for ALL. These numbers are lower than those reported in many African series [10]. Thrombocytopenia is an important sign visible on the blood count, linked to a lack of megakaryocytes, hindering regular production. It serves not only as a diagnostic and prognostic factor, but also as a therapeutic monitoring indicator [16].

4.4. Therapeutic and Prognostic Aspects

The management of acute leukemias is based on several factors. For ALL, frontline treatment primarily involves a dose-intensity concept, in line with the very acute nature of this neoplasm, which is one of the most aggressive in the short term but has a complete remission of induction rate close to 80% [17]. As for AML, they represent therapeutic emergencies due to disease- and treatment-related complications. Current treatments are based on combination chemotherapy (anthracycline and cytarabine) aiming to achieve complete remission during induction. Recent advancements have led to a better understanding of the different AML subtypes and the proposal of tailored treatments, including targeted therapies, such as retinoic acid in AML3 [18]. Hence, we selected the MARALL protocol for ALL cases and the AML 99 protocol for AML cases, treating 52% of patients over 2 years. Ngamai B. in Burkina Faso had treated 18.2% of cases [4]. After induction, 73% of ALL and 37% of AML patients achieved complete remission in our study.

Patient Survival

The average overall survival of our patients was 16.223 months (±3.191). This low rate could be explained by delayed diagnosis and especially by the stage of complications. This situation is also observed by many African authors, including Ngamai B. *et al.* in Burkina Faso and Ouedraogo RC at the YO University Hospital in Ouagadougou [4] [7]. Patients with AML had a lower average survival than those with ALL (6.853 ± 1.200 months vs. 21.720 ± 5.920 months). According to the literature, over the past 10 years, the treatment consensus for AML has relied on the repeated use of high-dose cytarabine alone or in combination with an anthracycline [19] [20]. The survival after allogeneic transplantation is 55% ± 4% (EORTC), 53% ± 5% (Blood 97), and 66% ± 16% (BGMT 87), and after autologous transplantation, it is 48% ± 5% (EORTC), 50% ± 5% (Blood 97), and 51% ± 17% (BGMT 87) [21]. As for ALL, the management has improved by drawing inspiration

from pediatric protocols based on a dose-intensity scheme with strict adherence to intervals between treatments and the use of molecules with strong anti-leukemic effects [22]. Overall survival varies among different authors, with rates of 34% at 5 years according to Lamanna *et al.* in 2013 with the ALL-2 protocol, 30% at 2 years according to Hunault-Berger *et al.* in 2010 with the GRALL SAI protocol, and 50% at 3 years according to Thomas *et al.* in 2010 with the modified Hyper-CVAD protocol [23]-[25].

5. Conclusion

Acute leukemia still remains a major problem in our context, due to the precariousness of limited financial, diagnostic and therapeutic resources. Thus reflecting in our results, the increasing number of cases, the diagnostic delay and the guarded prognosis. This is the reality in several other countries in the sub-region and even in certain developed countries.

Thanks

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Conflicts of Interest

No conflicts of interest.

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