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# PROFILE OF ACUTE LEUKEMIAS AT CHEIKH ZAID INTERNATIONAL UNIVERSITY HOSPITAL IN RABAT: STUDY OF 66 CASES

**Hadi Imane*, Nader Soufiane, Wali Alami Mohammed, Iraqui Houssaini Zineb and Belmekki Abdelkader**

Rabat, Morocco., Department of Medical Laboratory Science, Cheikh Zaid International University Hospital of Health Sciences, UIASS.

***Corresponding Author: Hadi Imane**

Rabat, Morocco, Department of Medical Laboratory Science, Cheikh Zaid International University Hospital of Health Sciences, UIASS.

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## ABSTRACT

Acute leukemias (AL) are severe malignant hematologic disorders characterized by uncontrolled proliferation of immature hematopoietic cells arrested at an early stage of differentiation in the bone marrow, leading to their spread into peripheral blood and secondary tissues. This retrospective and descriptive study analyzes the epidemiological, clinical, cytological, immunophenotypic, cytogenetic, and molecular characteristics of 66 patients diagnosed with acute leukemia at the Medical Biology Laboratory of Cheikh Zaid International University Hospital (HUICZ) in Rabat.

**KEYWORDS:** Acute leukemias, epidemiology, cytogenetic, molecular biology, immunophenotyping.

## ABREVIATIONS

AL: Acute leukemias
ALL: Acute lymphoblastic leukemia
AML: Acute myeloid leukemia
HUICZ: Cheikh Zaid International University Hospital
CML: Chronic myeloid leukemia
MCH: Mean Corpuscular Hemoglobin
MCV: Mean corpuscular volume
MDS: Myelodysplastic syndrome

## INTRODUCTION

Acute leukemias constitute a heterogeneous group of hematologic conditions that require urgent therapeutic intervention.[1] They are classified into acute myeloid leukemia (AML), more common in adults[2], and acute lymphoblastic leukemia (ALL), predominantly found in children.[3] Advances in diagnostic techniques, particularly immunophenotyping and cytogenetics, have greatly improved the understanding of prognostic factors and genetic abnormalities associated with these diseases. This study aims to describe these characteristics in a Moroccan population treated at HUICZ in Rabat and to compare the results with international data.

## MATERIALS AND METHODS

A retrospective descriptive study was conducted on 66 patients with confirmed acute leukemia based on cytological examination (bone marrow analysis) and complementary tests (immunophenotyping, karyotype, and molecular biology).

The blood smears were read by the professor of hematology, the medical biologist and the resident.

Myelograms were read by the professor of hematology.

Immunophenotyping, karyotyping and molecular biology were subcontracted (Biomnis, Cerba), and the technician managed the shipments.

Epidemiological, clinical and biological data were extracted from patients medical records.

In our series, we included patients of both sexes with myelogram-confirmed acute leukemia. Patients with no clinical records were excluded.

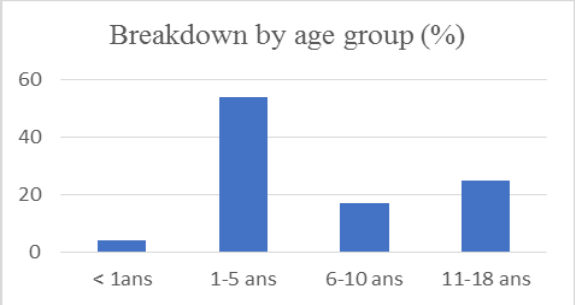


**Figure 1: Distribution of Acute Leukemias by Age Group in Children.**

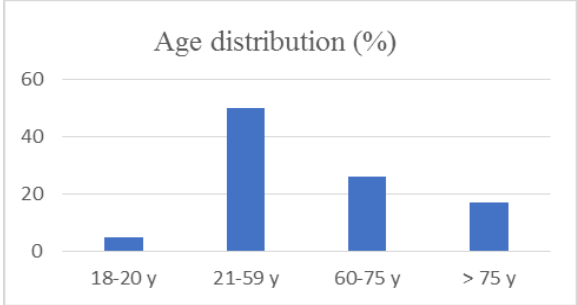


**Figure 2: Distribution of Acute Leukemias by Age Group in Adults.**

## RESULTS

### 1. Epidemiological data

**Age and distribution of patients**: Patient age ranged from 11 months to 83 years, with a mean of 36 years.
33% of patients were children (11 months - 17 years) and 67% adults (over 18 years).

The mean age of all ALL cases combined was 16 years. Children (21 cases) accounted for 75% of cases, with extremes ranging from 11 months to 16 years.

The mean age of AML cases combined was 51 years, of which 92% were adults (35 cases) aged between 20 and 83 years.

**Sex Distribution**: A male predominance was observed, with an overall male-to-female ratio of 2.6.
Among children, the ratio was 5:1, while in adults, it was 2:1.

### 2. Clinical circumstances

**Clinical presentation**

- **Medullary insufficiency syndrome**: 47% of patients presented an anemic
syndrome, marked by pallor and fatigue, 27% a hemorrhagic syndrome (petechiae, ecchymosis, mucosal bleeding) and an infectious syndrome (fever, recurrent infections) was observed in 20% of cases.
- **Tumor syndrome**: 40% of our patients had a tumor syndrome.
- **Incidental findings**: 4 cases were discovered incidentally.

### 3. Biological results

- **Blood count**

***Hemoglobin:*** Hemoglobin ranged from 2.04 g/dI to 13.58 g/dl, with a mean of 8.4 g/dl and a median of 8.63 g/dl.
MCV values ranged from 70.5 to 113 fl.
MCH ranged from 16.3 to 36 pg.
Reticulocytes ranged from 2,768 to 103,360/mm 3.
66% of our patients had normochromic normocytic anemia, 18% had microcytic hypochromic anemia, 8% had macrocytic anemia and 8% had no anemia.

***White blood cells:*** WBCs ranged from 600 to 420,000 elements/$mm^3$.
Hyperleukocytosis with WBCs between 10,000 and 50,000 elements/$mm^3$ was found in 29% of our patients, major hyperleukocytosis with WBCs > 50,000/$mm^3$ was observed in 53% of cases, while 31% of patients had leukopenia (WBC < 4000/$mm^3$).

***Platelets:*** Platelets ranged from 6,000 to 393,000 elements/$mm^3$.
66% of patients had severe thrombocytopenia with platelet counts below 50,000/ul.

***Circulating blasts:*** The mean rate of circulating blasts was 42%, with values ranging from 0% to 95%.
Average circulating blasts were 48% for ALL and 36% for AML.

- **Myelogram**

- Marrow blast rates: In children, bone marrow blast rates ranged from 25% to 95% (mean 84%), while in adults, rates ranged from 25% to 96% (mean 72%).

The blast rate for ALL was 85%, compared with 69.5% for AML.

- MPO cytochemistry: performed on all bone marrow smears in our series:
  - Negative in all cases of ALL and in 5% of AML.
  - Positive in 75% of AMLs.
  - Double population (negative, positive) in 20% of AMLs.
- Cytological and histochemical aspects:
  - 28 ALL (42.5% of patients), including 4 Burkitt's leukemias.
  - 38 AML (57.5% of patients)

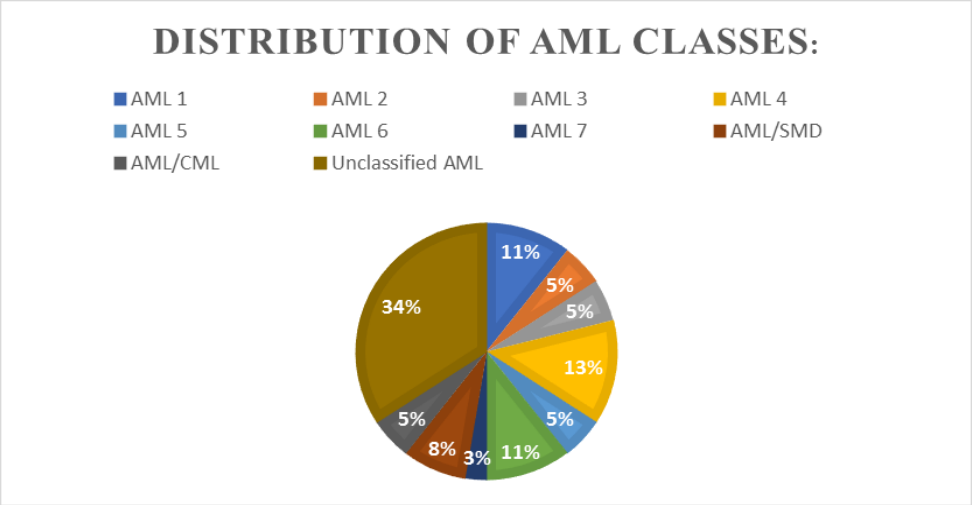


**Figure 3: Distribution of AML Cases by Subtype.**

- **Immunophenotyping**: Performed only on 36 patients,

Among the ALLs, 10 cases were B cell ALL and 5 were T cell ALL.
Immunophenotyping classifies the AMLs as follows:
- 14 AML
- 3 AML with monocytic component
- 2 MPO-positive AML.
- 1 AML with expression of the CD 19 marker.
- 1 AML with aberrant CD7 expression

- **Cytogenetic Analysis**

Karyotypes were performed in 42 of 66 cases, and the chromosomal abnormalities found were:
For AML:
- 11 AML with normal karyotype
- 3 AMLwith hyperploidy
- 2 AML with t(8;21)(q22;q22); *(AML1/ETO)(RUNX1/RUNX1T1)*
- 2 AML with complex karyotype
- 2 AML with hypoploidy + monosomy of 7
- 2 AML with isolated trisomy 8
- 1 AML with loss of Y
- 1 AML with t(9;22)
- 1 AML with t(15;17)
- 1 AML with t(11;19)
- 1 AML with rearrangement 12p13; t(X,3)

**For ALL**
- 6 ALL with normal karyotype
- 2 ALL with t(1;19)
- 1 ALL with t9;22)
- 1 ALL with Hyperdiploidy 54 chr
- 1 ALL with Hyperdiploidy 47 ch + Trisomy 10
- 1 ALL with Hypodiploidy
- 1 ALL with t(12;21)(p13;q22); TEL-AML1 (ETV6-RUNX1)
- 1 ALL with t(8;14)(g24;q11)

- **Molecular biology**

22 cases out of 66 underwent molecular biology and the molecular abnormalities found were: For AML:
- 7 AML with normal molecular biology (Negative for NMP1, FLT3, CEBPA, DNMTA)
- 3 AMLs with MPM1 +
- 2 AML with FT3 +
- 1 AML with bcr-abl transcript
- 1 AML with NMP1+, FLT3+, CEBPA+, DNMT3A+
- 1 AML with KRAS, TET and SRSF2 mutations
- 1 AML with DNMT3A, TP53 +.
- 1 AML with EVIl +
- 1 AML with CEBPA+.

**For LAL**
- 3 ALL with normal molecular biology
- 1 ALL with presence of bcr-abl transcript

## DISCUSSION

Acute leukemia (ALL) is a hematological emergency requiring rapid identification and appropriate therapeutic management. Our retrospective study of 66 patients describes the main epidemiological, clinical and biological features of acute leukemia at Cheikh Zaid University Hospital in Rabat. The results obtained show similarities but also peculiarities in comparison with international and Moroccan studies.

- **Epidemiological aspects**

Childhood ALL is the leading cause of pediatric cancer (30%), occurring mainly before the age of 9. In Europe and the United States, ALL accounts for 75-80% of leukemias and around 20% of cancers in children under 15 (4). Around 75% of cases occur in patients under the age of 18, with a peak in frequency between the ages of 2 and 5 (5).

Indeed, ALL preferentially affects extreme ages, with a bimodal distribution of incidence and mortality (< 15 years and > 80 years) (6).

In adults, on the other hand, they are four times rarer than AML (around 5% of leukemias) (2).

**Table I: Comparison of mean age in our series with other series in the literature.**

| Series<br>Average age | Casablanca (7) | Marrakech (8) | France (9) | Brazil (10) | Our serie |
|---|---|---|---|---|---|
| **LAL** | 21 years old | 13.8 years | 25 years old | 9 years old | 16 years old |
| **LAM** | 38 years old | 35.3 years | 63 years old | 34 years old | 51 years old |

In our series, 28% of AL cases occurred at less than 10 years of age, and 90% of these were of the lymphoblastic type.

However, our series included only 3 confirmed cases of childhood AML.

Age is an important prognostic factor, and is associated with poor evolution when it is less than one year or more than 10 years.[11],[12]

In our series, 29% of children had a poor prognostic age (4% aged under 1 year and 25% aged over 10 years). The children most affected are between 1 and 10 years of age (57% of children), with a peak in frequency at 5 years of age. This is identical to the literature, which states that AL (especially ALL) more often affects children under 10 years of age.[6],[14]

AML tends to be a disease of the elderly, with an average age of 63 and a marked increase in incidence from the age of 60 on wards.[3] Age > 60 carries a poor prognosis. In our series, 43% of adults were aged over 60.[15]

Our study also revealed a male predominance, with an overall sex ratio of 2.6, which is in line with the majority of studies on acute leukemias. Studies conducted in the USA and Europe report sex ratios ranging from 1.2 to 1.5 in favor of men, reinforcing the idea that acute leukemias affect men more frequently than women. In our series, this ratio was particularly marked in children (sex ratio of 5), in line with data reported in other pediatric studies where male sex is a predominant risk factor for lymphoblastic leukemia.

**Table II: Comparison of sex ratio in our series with other literature series.**

| Series | Tunisia[13] | Brazil | India | Our serie |
|---|---|---|---|---|
| Sex ratio | 1,27 | 1,48 | 2,1 | 2,6 |

- **Clinical circumstances**

The main clinical manifestations in our series were dominated by the anemic syndrome (47%), the tumor syndrome (40%), and the hemorrhagic syndrome (27%).

- **Medullary insufficiency syndrome**

**a/ Anemic syndrome**

It is a subjective syndrome, more or less appreciated depending on the case, dominated by a cutaneous-mucosal pallor of variable intensity depending on the precocity of the consultation and the extent of the hemorrhage thatmay be associated with it.

In our series, 47% of cases had an anemic syndrome at diagnosis, whereas in the series by Sintha et al, 71% of patients had an anemic syndrome.[16],[17]

Pallor is found at diagnosis in 84% of childhood ALL.[18]

**b/ Hemorrhagic syndrome**

The haemorrhagic syndrome may consist of cutaneous, mucosal or visceral haemorrhages, sometimes revealing AML.[16] It was present in 27% of cases in our study.

In a study of 281 patients carried out at a Tunisian center between 1998 and 2008, 15% of patients had a hemorrhagic syndrome[19], while it was present in 21% of cases in a study by Sintha et al in India.[20]

**c/ Infectious syndrome**

Fever reveals an infectious syndrome described as the most frequent clinical presentation at diagnosis.[21] It can vary in intensity.

In our series, the infectious syndrome was present in 20% of cases. In the series by Rego et al in Brazil[10], 58% of patients had an infectious syndrome at diagnosis, while Sintha et al in India report a higher frequency of around 80%.

Before any treatment, fever requires biological and bacteriological tests to identify its origin and the causative germ, and to institute effective antibiotics. In the absence of a precise infectious focus, fever is associated with the disease itself.[22]

- **Tumor syndrome**

It is more frequent in ALL (almost constant) than in AML (50% of cases)[23], and is a consequence of the leukemic tumor mass.[17]

In our series, it was only found in 40% of cases.

Gingival hypertrophy is a frequent feature of ALL, occurring in 40% of cases in myeloid leukemias (especially monoblastic varieties) and only 20% in lymphoid leukemias.[24] In our series, it was present in a patient with AML4.

- **Biological aspects**

The results of the blood count in our study show a significant prevalence of anemia in 93% of patients, with hyperleukocytosis in 53% and leukopenia in 31%. These

results are in line with international data, where anemiais frequently observed at diagnosis of acute leukemia.

Hyperleukocytosis, particularly in myeloid leukemias, is a major prognostic factor and is associated with an increased risk of complications such as leukostasis syndromes and disseminated intravascular coagulopathy (DIC). The hyperleukocytosis found in our series is associated with an increased risk of complications such as leukostasis syndromes and disseminated intravascular coagulopathy (DIC). The hyperleukocytosis found in our series is relatively high compared with other international studies, where the prevalence varies between 40% and 50%. This may be linked to delayed diagnosis or late management of patients, leading to more advanced blast proliferation.

The most important element in establishing the diagnosis of LA on the blood count is the presence of circulating blast cells. Absence of blast cells does not mean absence of LA, but rather absence of blood invasion by blast cells.[25]

In our series, the rate of circulating blasts ranged from 0% to 95%, with an average of 42%.

In our series, the average number of bone marrow blasts was higher in children (84%) than in adults (72%)

The medullary blast rate is usually over 90% in ALL[18]; in our series, the mean blast rate for ALL was 85%.

The most rapid and informative cytochemical reaction is myeloperoxidase (MPO). Its positivity (≥ 3% of blasts showing reactivity) helps to rule out or confirm the myeloid origin of blasts.[26] This staining is therefore particularly useful and has enabled us to distinguish myeloblastic leukemia without maturation or with minimal maturation from acute lymphoblastic leukemia.

In our series, the diagnosis of AML was retained in 95% of cases.

- **Immunophenotyping and cytogenetics**

Immunophenotyping by flow cytometry uses antibodies (CD: Differentiation Cluster) to identify membrane antigens.

Three major immunophenotypic groups have been identified in ALL: the pre-B phenotype making up 70-80%, the T phenotype (15%) and the mature B phenotype corresponding to Burkitt-type leukemias (2-5%). The T phenotype appears to be more frequent in developing countries.[27]

In our series, 36/66 patients had undergone immunophenotyping, which discriminated between B- and T- ALL in 15 patients.

This technique was also used to type 3 AMLs with a monocytic component.

The role of cytogenetics in the management of acute leukemias is now widely recognized (28)(50). Studies of these genes have revealed that they are often directly or indirectly involved in blood cell development and homeostasis, and that abnormal fusion gene protein products created by specific translocations and inversions can deregulate blood cell proliferation, differentiation or programmed cell death (apoptosis).[28] This has paved the way for new therapeutic agents targeting specific genetic abnormalities in blasts, such as the tyrosine kinase inhibitor imatinib, which blocks the proliferation of cells with the *BCR-ABL* fusion gene transcribed from t(9;22) (q34;q11.2), a chromosomal aberration recurrent in chronic myeloid leukemia (CML) but also in ALL.[29]

Moreover, cytogenetic analysis is now an integral part of the diagnosis and prognosis of AML[30] and ALL , and chromosomal abnormalities and their molecular homologues have been included in the World Health Organization (WHO) classification of hematological malignancies.[31][32]

In our series, karyotyping was performed in only 63% of patients and was normal in 42%

The most frequent cytogenetic abnormalities in AML were hyperploidy, t(8;21)(q22;q22), complex karyotype, hypoploidy and isolated trisomy 8.

These results are in line with those found in a study in Ohio, USA.[33]

Two patients with ALL had t(1;19). It accounts for 2-3% of chromosomal abnormalities in adult ALL[59][60][100][64], in whom it has a poor prognosis.[34][35]

In children, they are more frequent (4- 5%)[36] and have a very good prognosis.

A t(9;22) was found in one patient with ALL. It represents the most frequent recurrent abnormality in adult ALL (11-29%).[59][54]

## CLASSIFICATION

The long-standing relevance of the FAB classification is attributed to its relative simplicity (10), based on a straightforward morphological description following MGG-stained blood and bone marrow smears, supplemented by cyto-chemical tests accessible to most laboratories. This method takes into account the cytological abnormalities of blood and bone marrow. Despite its limitations, this approach remains the cornerstone for acute leukemia (AL) diagnosis in clinical settings.

Indeed, the FAB classification is still routinely employed for initial diagnosis when data regarding specific

biological subtypes are unavailable, particularly in cases of acute promyelocytic leukemia (APL, AML-M3). AML-M3 is characterized by a typical clinical presentation, including a pronounced hemorrhagic syndrome (cutaneous and mucosal), sometimes severe (e.g., intracranial hemorrhage), due to disseminated intravascular coagulation (DIC) and aberrant fibrinolysis activation. This scenario constitutes a therapeutic emergency, necessitating urgent diagnosis (within hours of admission) to initiate specific treatment and avert rapid mortality risk.[37]

In our series, classifying ALs based on morphological and cyto-chemical criteria posed challenges in some cases. This underscores the need to characterize blast populations using additional immunological and cytogenetic markers to confirm or refine diagnoses and better tailor therapeutic strategies.

Integrating blood and bone marrow smear analysis with surface membrane molecule studies is critical for diagnosing complex cases. Flow cytometry remains the gold-standard technique for immunophenotyping in acute leukemias. The primary objectives of immunophenotyping include detecting abnormal cells, determining their lineage, analyzing their heterogeneity, and characterizing their phenotypic features.

When blasts exhibit no morphological signs of myeloid differentiation, immunophenotyping is the only method to confirm their myeloid origin. Similarly, molecular biology has become an essential tool in AL evaluation, particularly for detecting cryptic translocations, analyzing karyotype failures, and assessing minimal residual disease.[38]

In our study, morphological analysis of blood and bone marrow smears, alongside myeloperoxidase staining, categorized ALs as:

- 58% AML**;**
- 42% ALL**.**

These results align with findings from various studies in the literature (Table III).

| | Casablanca | Tunisia | Valence | Our serie |
|---|---|---|---|---|
| **AML** | 64 | 51 | 82,7 | 57,5 |
| **ALL** | 30 | 40 | 15 | 42,5 |

Table III : Comparison of frequencies (%) of AML and ALL

**Acute Myeloid Leukemia (AML)** constitutes 1% of cancers and 80% of adult acute leukemias, with increasing incidence. Among children, AML accounts for only 10–15% of ALs and is rare before the age of 15.[17] In our series, AML was the most common type, representing 58% of acute leukemias. Similarly, in Lower Normandy[18], 72% of ALs were AML. At Valence Hospital, the frequency was even higher at 82%.[14]

Cytologically, subtypes M1 and M2 are the most prevalent, representing approximately 30% and 20%, respectively. While AML-M6 is rare (3–5%), it accounts for up to 20% of secondary Als.[23]

Cytological features in AMLs do not predict prognosis. Some studies report higher complete remission rates in categories M1, M2, and M3 compared to M4, M5, and M6 forms, though these findings are not universally corroborated. Prognostic classifications have evolved significantly with the advent of cytogenetics and molecular biology.

In a study by Sintha et al. in India[20], AML-M2 was the most frequent subtype (59%), followed by AML-M4. At Valence Hospital, M2 was also predominant (21%), followed by M5 and M4.

At Casablanca University Hospital[7], cytological analysis revealed higher frequencies of AML-M1 and M2 (31% and 28%, respectively) compared to Tunisia[13] (12% and 17%, respectively).

Our study findings were consistent with other series, with AML-M1 and M4 being the most common subtypes.

In our series, 20% of AML cases could not be classified cytologically, compared to 10% in a study from Casablanca.[7]

**Acute Lymphoblastic Leukemia (ALL):** Among children, ALL accounts for 75–80% of leukemias and 25% of all cancers. It occurs in 75% of cases before the age of 6.[5]

The L1 subtype is the most common in pediatric ALL.

The L1 and L2 varieties are not fundamentally distinct but differ in the proportions of shared blast cells. The prognostic value of L2 compared to L1 has not been demonstrated.

The FAB L1/L2 subclassification has lost significance with the advent of immunological and molecular subclassifications.

In our series, 14% of ALL cases were of the L3 subtype. Distinguished by the cytoplasmic characteristics of Burkitt cells, this form is rare, occurring in 9.7% of adult ALL cases and 2–4% in children.[40] According to the 2008 WHO classification, these forms are categorized as mature B-cell neoplasms.

## CONCLUSION

The management of acute leukemia (ALL) in Morocco presents challenges linked to the lack of certain advanced diagnostic techniques. For overall improvement, it is recommended to strengthen flow cytometry units and capacities in cytogenetics and molecular biology. The

creation of a national cancer registry is also essential for monitoring disease trends and adapting treatment protocols. In addition, raising professional awareness of the importance of properly documenting clinical records, improving dialogue between clinicians and biologists through multidisciplinary meetings, and setting up a computerized medical record system are priority measures for optimizing patient care.

**Declaration of Conflict of Interest:** The authors declare that the research has no commercial or financial relationships that could be construed as a potential conflict of interest.

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**Authors' Contributions:** We confirm that the submitted manuscript is original, has not been published elsewhere, and is not under consideration by any other journal. All authors have significantly contributed to this research, approved the final manuscript, and agreed to its submission.

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