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Research Article

The Role of the Complete Blood Count in the Diagnosis of Chronic Lymphocytic Leukemia: A Retrospective Series

Hajar Jamii[1,2]*, Elhoucine Ait Amar[1,3], Abdelkarim Amagour[1,2], Ilham Orchi[1,2] and Hafid Zahid[1,2]

[1]*Laboratoire d'hématologie et Immunohématologie, HMIMV, Rabat, Morocco*

[2]*Faculté de Médecine et de Pharmacie, Université Mohammed V, Rabat, Morocco*

[3]*Faculté de Médecine et de Pharmacie, Université Moulay Ismail, Errachidia, Morocco*

***Corresponding Author:** Hajar Jamii, Faculté de Médecine et de Pharmacie, Université Mohammed V, Rabat, Moracco.

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Abstract

Introduction and Aim: Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults in Western countries and predominantly affects the elderly. Diagnosis relies on immunophenotyping, yet the complete blood count (CBC) and peripheral blood smear provide essential initial diagnostic clues through the identification of persistent monomorphic lymphocytosis and characteristic Gumprecht shadows. This study aims to evaluate the contribution of the CBC and peripheral blood smear in the diagnosis of CLL in Mohammed V Military Training Hospital (HMIMV) in Rabat, Morocco.

Methods: A retrospective study was conducted on 16 patients diagnosed with CLL at HMIMV, Rabat, Morocco, from February 2020 to August 2025. CBC parameters, blood smear findings, and demographic data were collected and analyzed.

Results: The mean age was 65 years (range: 47-87), with an equal sex ratio. The mean white blood cell (WBC) count was 118.7 G/L and mean lymphocyte count was 116.12 G/L. Anemia was present in 87.5% of patients and thrombocytopenia in 43%. Blood smear examination revealed monomorphic lymphocytosis in all cases, Gumprecht shadows in 93.75%, and prolymphocytes in 31.25%. Notably, 25% of patients were under 55 years of age.

Conclusion: The CBC and peripheral blood smear are fundamental tools for the initial diagnosis of CLL. Our data suggest a higher tumor burden and more advanced disease at presentation, likely attributable to diagnostic delays. These findings highlight the importance of systematic hematological screening in at-risk populations.

Keywords: *Chronic Lymphocytic Leukemia; Complete Blood Count; Lymphocytosis; Gumprecht Shadows; Peripheral Blood Smear; Morocco*

Introduction

Chronic lymphocytic leukemia (CLL) is a B-cell malignancy characterized by the accumulation and clonal proliferation of mature malignant B lymphocytes in the peripheral blood, bone marrow, and lymphoid organs. It is the most common adult leukemia in many countries, with an age-adjusted incidence of 4.6 per 100,000 inhabitants per year, a median age at diagnosis of 70 years, and an estimated 20,700 new cases per year in the United States [1]. Its incidence is significantly lower in Asian and Middle Eastern populations, and robust epidemiological data from North Africa and Sub-Saharan Africa remain scarce [2,3].

The diagnosis of CLL is established by demonstrating a peripheral blood B-lymphocyte count ≥ 5 × 10^9/L for a duration of at least 3 months, with a characteristic immunophenotype (CD5+, CD19+, CD23+, CD20dim, sIgdim) according to the 2018 iwCLL guidelines. Although flow cytometric immunophenotyping remains the gold standard for definitive diagnosis, the complete blood count (CBC) and peripheral blood smear represent readily accessible and cost-effective first-line investigations that can strongly orient the clinician toward the diagnosis [1,4]. The cardinal CBC finding in CLL is a persistent absolute lymphocytosis, frequently accompanied by anemia and thrombocytopenia that reflect bone marrow infiltration or autoimmune mechanisms. On peripheral blood smear, the leukemic cells appear as small, mature lymphocytes with dense, clumped chromatin and scant cytoplasm.

A hallmark morphological feature, specifically mentioned in the 2018 iwCLL diagnostic criteria, is the presence of Gumprecht nuclear shadows (smudge cells), artifacts produced by the mechanical fragility of malignant CLL lymphocytes during smear preparation. Beyond their diagnostic value, the quantification of smudge cells on routine blood smears has been shown to carry independent prognostic significance [5,6].

In resource-limited settings, CLL is frequently diagnosed at advanced stages owing to limited access to routine hematological screening and delayed medical consultation. This has been quantified at the global level, demonstrating that while approximately 50% of patients in high-income countries present at early Binet stage A, only 9-18% do so in low and middle-income countries [3]. Data specifically describing the clinicohematological profile of CLL in Morocco and the broader North African region remain scarce.

Objective of the Study

The objective of the present study was to describe the diagnostic contribution of the CBC and peripheral blood smear in CLL at a Moroccan military training hospital, and to compare our findings with published data from African, Asian, Middle Eastern, and Western series.

Materials and Methods

Study approach and patient selection

This was a retrospective and descriptive study conducted in the Department of Hematology and Immunohematology at Mohammed V Military Training Hospital in Rabat, Morocco. All patients diagnosed with CLL during the period from February 2020 to August 2025 were included, regardless of age, sex, or mode of referral (hospitalized or outpatient). Diagnosis was established according to standard criteria, combining CBC findings, peripheral blood smear morphology, and flow cytometric immunophenotyping of peripheral blood lymphocytes. Patients with insufficient diagnostic data or lost to follow-up before confirmation of diagnosis were excluded.

Data collection and analysis

Clinical and biological data were retrospectively extracted from the laboratory information system and patient medical records. The following variables were recorded: age at diagnosis; sex; CBC parameters from the most recent hemogram at or prior to diagnosis (white blood cell count [WBC], hemoglobin [Hb], platelet count, absolute lymphocyte count); peripheral blood smear findings (lymphocyte morphology, presence of Gumprecht shadows, prolymphocyte percentage); and immunophenotyping results where available. Anemia was defined as hemoglobin < 13 g/dL in men and < 12 g/dL in women. Thrombocytopenia was defined as a platelet count < 100 × 10^9/L. Young CLL patients were defined as those aged ≤ 55 years, consistent with prior literature [4]. Gumprecht shadows were defined as the smudge-cell artifacts on the peripheral blood smear resulting from the mechanical fragility of malignant lymphocytes during slide preparation.

Data analysis

Statistical analysis was carried out using two-way analysis of variance (ANOVA) with $\alpha = 0.05$. All analyses were conducted using SPSS software.

Results

Over the 5.5-year study period (February 2020 - August 2025), 16 patients were diagnosed with CLL at HMIMV. The sex ratio was equal, with 8 males (50%) and 8 females (50%). The mean age at diagnosis was 65 years (range: 47 - 87 years). The age distribution by decade showed the following groups: 40 - 49 years (n = 1), 50 - 59 years (n = 5), 60 - 69 years (n = 5), 70 - 79 years (n = 3), and 80 - 89 years (n = 2). Four patients (25%) were aged 55 years or younger (young CLL), while 12 patients (75%) were over 55 years of age (Figure 1).

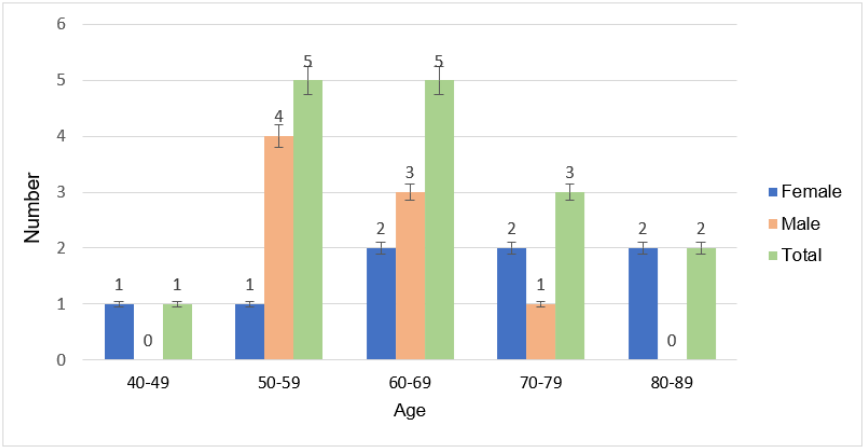

Figure 1: *Age and sex distribution of patients with chronic lymphocytic leukemia.*

Table 1 presents the mean values of the main CBC parameters recorded at the time of diagnosis.

Variable	Mean (Range)/n (%)
Age (years)	65 (47 - 87)
Sex - Female	8 (50%)
Sex - Male	8 (50%)
White blood cells (G/L)	118.7 (19.7 - 342.4)
Hemoglobin (g/dL)	9.81 (5.1 - 13.5)
Platelets (G/L)	178.75 (62 - 369)
Absolute lymphocytes (G/L)	116.12 (8.1 - 304.74)

Table 1: *Mean values of the main CBC parameters.*

The mean WBC count was 118.7 G/L (Range: 19.7 - 342.4 G/L) with a corresponding mean absolute lymphocyte count of 116.12 G/L (Range: 8.1 - 304.74 G/L). The mean hemoglobin was 9.81 g/dL (Range: 5.1 - 13.5 g/dL). Anemia was detected in 14 out of 16 patients (87.5%). Thrombocytopenia was present in 7 patients (43%), with a mean platelet count of 178.75 G/L (Range: 62 - 369 G/L).

Peripheral blood smear examination revealed a monomorphic lymphocytosis composed of small mature-appearing malignant lymphocytes in all 16 patients (100%). Gumprecht shadows (smudge cells) were identified in 15 patients (93.75%). Prolymphocytes were observed in 5 patients (31.25%), and in all cases their proportion was below 10% of the total lymphoid population, consistent with typical CLL morphology (Figure 2). Peripheral blood smear findings are summarized in table 2.

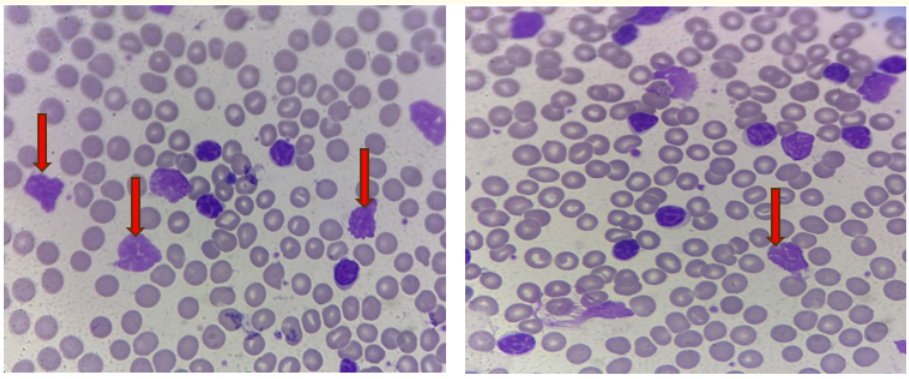

Figure 2: *Peripheral blood smear of chronic lymphocytic leukemia showing lymphocytosis with a population of small mature lymphocytes with Gumprecht shadows (Smudge cells).*

Peripheral Blood Smear Finding	n (%)
Monomorphic lymphocytosis (small mature lymphocytes)	16 (100%)
Gumprecht shadows (smudge cells)	15 (93.75%)
Prolymphocytes (proportion < 10%)	5 (31.25%)

Table 2: *Peripheral blood smear findings in CLL patients at the time of diagnosis (n = 16).*

Discussion

This retrospective study reports the clinicohematological profile of 16 CLL patients diagnosed at a Moroccan military training hospital and assesses the diagnostic value of the CBC and peripheral blood smear. Our data reveal a clinically significant pattern of advanced disease at first presentation, contrasting markedly with contemporary experience. According to the global burden analysis by Ou, Long [3], only 9-18% of patients in low sociodemographic index (SDI) countries present at early Binet stage A, compared to approximately 50% in high-income countries, a disparity attributed primarily to the absence of routine blood count screening. Our series provides a concrete illustration of this reality in the North African context. Regarding epidemiological characteristics, the mean age at diagnosis in our cohort was 65 years, five years younger than the median of 70 years reported in Western populations by Hallek [1] in the 2025 CLL update. Furthermore, the sex distribution in our series was perfectly equal (M:F = 1:1), standing in marked contrast to the consistent male predominance of approximately 1.9:1 described in Western series, and the even higher M:F ratio of 4.66:1 reported by Sall, Touré [2] in the Senegalese cohort. This equal sex distribution may partly reflect referral patterns specific to a military teaching hospital, where

a greater proportion of civilian female patients is seen alongside military personnel; selection bias cannot be excluded. Notably, 25% of our patients were aged ≤ 55 years, a proportion substantially exceeding the 5 - 11% reported in European and North American series by Parikh, Rabe [7], and consistent with data from other non-Western settings. Alshemmari, Hamdah [8], in a retrospective study of 219 CLL patients from Kuwait Cancer Center, reported a median age of 59 years with 32% of patients aged ≤55 years and a similar attenuation of male predominance. Parikh, Rabe [7] in a comprehensive Mayo Clinic analysis of 844 young CLL patients (≤ 55 years), demonstrated that younger patients more frequently harbor adverse prognostic markers, including unmutated IGHV status and ZAP-70 overexpression, underscoring the importance of complete biological workup in this subgroup. These converging data suggest that the ≤ 55-year threshold represents a clinically and epidemiologically meaningful cutoff in non-Western populations that deserves heightened diagnostic attention.

The mean WBC count of 118.7 G/L and mean absolute lymphocyte count of 116.12 G/L in our series reflect a markedly elevated tumor burden at the time of presentation. These values substantially exceed the mean WBC (70.6 G/L) and lymphocyte count (51.4 G/L) reported by Agrawal, Naithani [9] in a comparable Indian retrospective series. In high-income countries, the introduction of systematic automated CBC analysis has progressively shifted CLL diagnoses toward the asymptomatic early stage: Hallek, Cheson [4] note that over 70% of newly diagnosed Western patients now present at Rai stage 0 or I, a pattern that is simply not replicated in the Moroccan cotext. The pathophysiological basis of sustained lymphocytosis in CLL involves impaired apoptosis, constitutive activation of the B-cell receptor (BCR) signaling pathway, and proliferative support from the tumor microenvironment [10]. It is worth noting that, in the context of targeted therapy, BCR-pathway inhibitors such as ibrutinib can induce a redistribution lymphocytosis through mobilization of malignant cells from lymphoid tissues to the peripheral blood; this phenomenon, which may persist beyond 12 months, should not be misinterpreted as disease progression, as demonstrated by Woyach, Smucker [11], though this consideration applies to patients already on treatment and is not relevant to the initial diagnostic setting of the present study.

Anemia, detected in 87.5% of our patients with a mean hemoglobin of 9.81 g/dL, is the most striking hematological finding of this series and represents the clearest indicator of advanced disease at first presentation. Under the 2018 iwCLL criteria, hemoglobin below 10 g/dL constitutes an indication for treatment initiation and defines Rai stage III and Binet stage C - both high-risk categories. This prevalence substantially exceeds figures from all comparative series: Ghosh, Singh [12] reported anemia in 26 - 43% of patients with lymphoid malignancies; Zeeshan, Sultan [13] found 26.7% in a Pakistani prospective cohort, with a thrombocytopenia rate of 21.7%; Dodhy, Zafar [14] reported 15.1% in a Pakistani decade-long retrospective series; Sriphatphiriyakun and Auewarakul [15] observed anemia in 54% of Thai patients; and Sall, Touré [2] reported 55% in Senegal. Our rate of 87.5% exceeds all published figures, strongly implying predominantly advanced-stage disease at first diagnosis in our population. The mechanisms underlying anemia in CLL are multiple and include direct bone marrow infiltration causing erythroid hypoplasia (the predominant cause in advanced disease), autoimmune hemolytic anemia (AIHA, which complicates 7-10% of CLL cases overall), and hypersplenism [12].

Thrombocytopenia was identified in 43% of our patients, exceeding the 18% in 184 Thai CLL patients, in whom thrombocytopenia was associated with significantly shortened overall survival [15], and the 21.7% reported in Pakistan [13]. In both the Rai and Binet classification systems, thrombocytopenia (platelet count < 100×10^9/L) defines high-stage disease, Rai stage IV and Binet stage C, and constitutes an indication for treatment. The concurrent finding of anemia in 87.5% and thrombocytopenia in 43% of our patients, representing bilineage bone marrow failure, is mutually reinforcing evidence that a large majority of our cohort presented with high-stage, bone marrow-infiltrative disease at the time of first diagnosis.

All 16 patients exhibited monomorphic lymphocytosis of small mature-appearing lymphocytes on peripheral blood smear, the morphological hallmark of CLL as defined by the 2018 iwCLL diagnostic criteria. Gumprecht shadows were identified in 93.75% of cases, closely comparable to the near-universal prevalence reported by Sall, Touré [2] in the Senegalese series, confirming that this morphological finding is a reliable diagnostic clue across diverse geographic settings. Beyond diagnosis, the quantification of smudge

cells carries independent prognostic significance. In a landmark Mayo Clinic study of 75 untreated early-stage CLL patients, Nowakowski, Hoyer [5] demonstrated that a smudge cell percentage exceeding 30% was significantly associated with mutated IGHV status, a longer time to first treatment ($p = 0.001$), and improved overall survival ($p = 0.04$). Prolymphocytes were present in 31.25% of cases, but their proportion remained below 10% in all patients, consistent with the typical CLL morphological subtype per the 2022 WHO classification of haematopoietic tumours.

Conclusion

The complete blood count and peripheral blood smear remain fundamental and accessible tools in the initial diagnostic workup of CLL. Our retrospective series of 16 patients confirms that the combination of persistent monomorphic lymphocytosis, characteristic Gumprecht shadows, and CBC-detected cytopenias constitutes a robust initial diagnostic orientation that should prompt immediate immunophenotyping for confirmation. Our data highlight several epidemiological particularities in the Moroccan context: a higher proportion of young CLL patients, a markedly elevated tumor burden, and a substantially higher prevalence of anemia and thrombocytopenia. These observations are consistent with a pattern of late-stage presentation at diagnosis, underscoring the urgent need for improved hematological screening programs and greater awareness of early CLL symptoms in North Africa. Systematic integration of the CBC in routine medical consultations; particularly in patients over 50 years of age presenting with unexplained fatigue, lymphadenopathy, or recurrent infections; could significantly reduce diagnostic delays and allow earlier therapeutic intervention. Future prospective multicenter studies are needed to characterize the full clinicobiological profile of CLL in Morocco and to assess its impact on treatment outcomes and overall survival.

Declaration of Interest

The authors declare that they have no competing interests.

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