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Challenges in the management of patients with chronic myelomonocytic leukemia in the Brazilian public healthcare system: from diagnosis to transplantation

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ABSTRACT

Chronic myelomonocytic leukemia (CMML) represents a diagnostic and therapeutic challenge in the Brazilian public healthcare system, particularly due to limited access to advanced diagnostic tools and disease-modifying therapies. A retrospective chart review was conducted, including patients diagnosed with CMML from 2015 to 2025 at a university hospital in northeastern Brazil. Fourteen patients were identified, with a mean age of 58.7 years, and 50% were male. At diagnosis, 57.1% were in the chronic phase and 42.9% in the acute phase. Only two patients (14.3%) received hypomethylating agents, and four (28.6%) underwent allogeneic hematopoietic stem-cell transplantation. The median overall survival for the cohort was 25 months. Patients diagnosed in the acute phase had a shorter median overall survival compared to those diagnosed in the chronic phase (8 vs. 25 months). A trend toward improved survival was observed among transplanted patients (25 vs. 8 months). Compared with contemporary data, patients in this cohort had lower exposure to hypomethylating therapy, although transplant-related characteristics and early engraftment outcomes were similar. Structural and therapeutic limitations within the public healthcare system may impact disease management and outcomes, reinforcing the importance of improving access to diagnostic resources, disease-modifying therapies, and timely referral for transplantation.

Keywords: Chronic myelomonocytic leukemia; Bone marrow transplantation; Hypomethylating agents.

INTRODUCTION

Chronic myelomonocytic leukemia (CMML) is a clonal myeloid neoplasm characterized by persistent monocytosis and biological overlap between myelodysplastic syndromes and myeloproliferative neoplasms. Although the reported incidence is below 1 per 100,000 persons per year, the burden of CMML is expected to rise with population aging, and the true epidemiology is probably underestimated because many historical cases were previously grouped with myelodysplastic syndromes.[1]

Current diagnostic and prognostic assessment of CMML relies on morphology, cytogenetics, molecular testing, and, in selected settings, monocyte-subset flow cytometry.[2-7] In the Brazilian public healthcare system, however, access to these resources is heterogeneous. This limitation may affect diagnostic confirmation, delay risk stratification, restrict access to disease-modifying therapies, and postpone referral for allogeneic hematopoietic stem-cell transplantation (HSCT), the only potentially curative treatment for eligible high-risk patients.[2-5]

In this context, the present study aimed to describe the clinical profile, treatment patterns, transplant journey, and survival of CMML patients followed over a 10-year period at a university hospital in Northeastern Brazil. A secondary objective was to contextualize institutional results against the Latin American transplant registry and selected contemporary CMML literature, emphasizing the practical challenges of diagnosis and treatment in the Brazilian public healthcare system.

METHODS

Study design and population

This was a retrospective, observational, single-center study based on chart review of patients treated from January 2015 to October 2025. Eligible cases were those with a documented diagnosis of CMML in institutional records and available clinical, therapeutic, and outcome data. Patients with an unconfirmed diagnoses or incomplete clinical, treatment, or outcome information were excluded. Documented CMML diagnoses were established by the treating hematology team according to the diagnostic resources available at the time of care. Before the institutional implementation of monocyte-subset flow cytometry, diagnosis relied on peripheral blood counts (hemogram) and bone marrow morphology (myelogram). After flow cytometry became available at the institution, a CMML-type monocyte repartitioning pattern with > 94% classical monocytes among total monocytes was used as an adjunct diagnostic criterion when available.[7]

Variables and data sources

Variables analyzed included demographics, baseline laboratory characteristics available in the records, disease phase at presentation, exposure to hypomethylating agents and other disease-directed therapies when documented, HSCT status, donor and graft characteristics, conditioning regimen, and neutrophil engraftment time when applicable. Data were manually extracted from institutional medical records and transplant follow-up records. Comparative benchmark data were extracted from the Latin American Bone Marrow Transplant Registry and selected contemporary CMML publications. These external comparisons were descriptive and were not intended as pooled or matched-control analyses.

Statistical analysis

Categorical variables were summarized as counts and percentages, and continuous variables were summarized using means and available ranges or medians, as appropriate to the information consistently retrievable from the historical dataset. Overall survival (OS) was estimated by the Kaplan-Meier method, from diagnosis to death from any cause or last documented follow-up. Survival curves were compared using the log-rank test. A two-sided $p < 0.05$ was considered statistically significant, and 95%CIs were adopted for survival analyses. Given the small sample size, all inferential analyses were considered exploratory.

Ethics

Ethics approval was granted under statement number 7.570.689 by the Research Ethics Committee of the Complexo Hospitalar, Universidade Federal do Ceará (opinion no. 7,570,689). The study was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent amendments.

RESULTS

The cohort comprised 14 patients with CMML. The mean age was 58.7 years, and 50% were male. Eight patients (57.1%) were diagnosed in the chronic phase and six (42.9%) in the acute phase. Two patients (14.3%) received hypomethylating agents, and four (28.6%) underwent HSCT. Among transplanted patients, the predominant conditioning regimen was reduced-intensity conditioning (RIC) with busulfan/fludarabine (BU/FLU) (Table 1).

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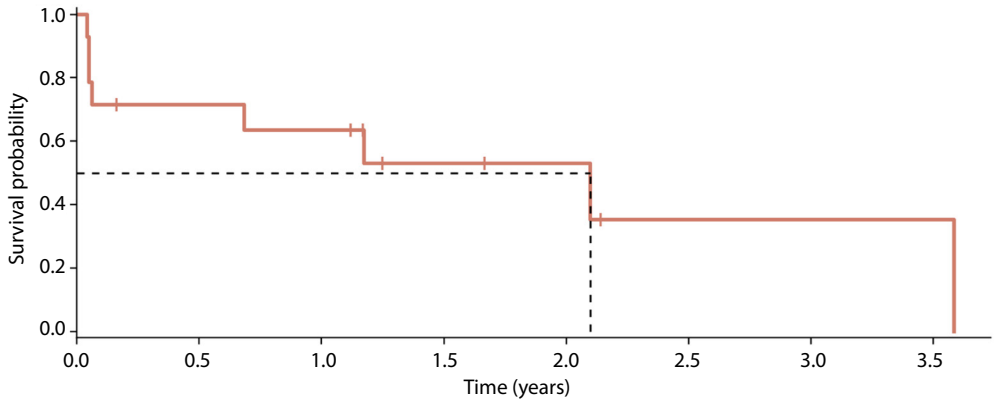
Table 1. General clinical and therapeutic characteristics of the institutional CMML cohort.

Characteristic	Value
Number of patients	14
Mean age, years (range)	58.7 (20-70)
Male sex, n (%)	7 (50.0)
Chronic phase at diagnosis, n (%)	8 (57.1)
Acute phase at diagnosis, n (%)	6 (42.9)
Underwent HSCT, n (%)	4 (28.6)
Received hypomethylating agents, n (%)	2 (14.3)
Other documented disease-directed therapy	Not systematically retrievable from historical records
Predominant conditioning regimen among transplanted patients	RIC (BU/FLU)

Source: Elaborated by the authors.

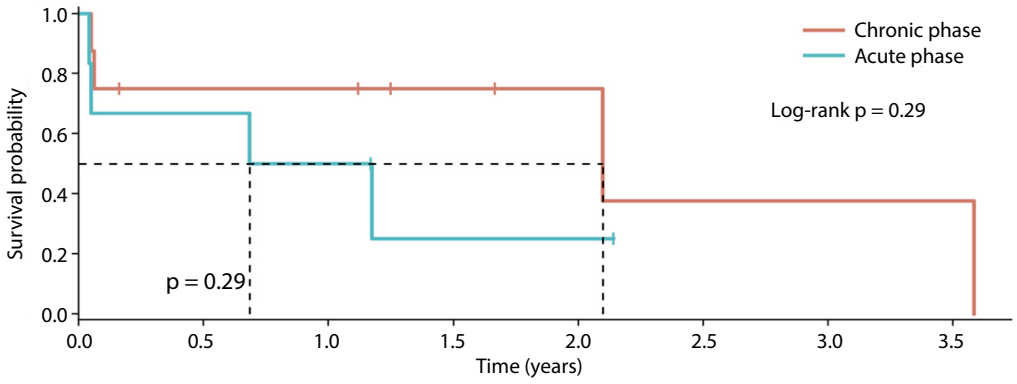
Median OS for the overall cohort was 25 months, with a steeper decline in the first 2 years after diagnosis (Fig.1).



Source: Elaborated by the authors.

Figure 1. OS curve of the cohort. Estimated median OS: 25 months, with a steeper decline in the first 2 years.

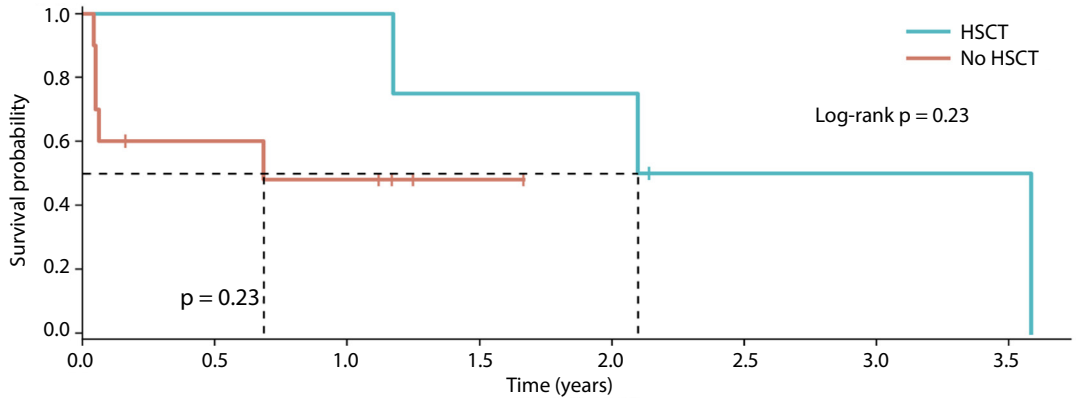
Patients diagnosed in the acute phase had shorter median OS than those diagnosed in the chronic phase (8 vs. 25 months), although this difference did not reach statistical significance (log-rank p = 0.29) (Fig. 2).



Source: Elaborated by the authors.

Figure 2. Kaplan-Meier OS according to disease phase at diagnosis (chronic phase vs. acute phase). Median OS was 25 months in chronic-phase cases and 8 months in acute-phase cases (log-rank p = 0.29).

A similar non-significant trend favored HSCT over no HSCT (median OS, 25 vs. 8 months; log-rank p = 0.23) (Fig. 3).



Source: Elaborated by the authors.

Figure 3. Kaplan-Meier OS according to treatment group (HSCT vs. no HSCT). Median OS was 25 months in transplanted patients and 8 months in non-transplanted patients (log-rank p = 0.23).

When institutional transplant-related characteristics were compared with selected contemporary CMML reports, our patients were younger and far less likely to receive hypomethylating agents, whereas donor type, graft source, conditioning approach, and neutrophil engraftment were broadly comparable among transplanted patients (Table 2).

Table 2. Institutional transplant-related characteristics vs. selected contemporary CMML literature.

Variable	University hospital	Selected literature
Mean age, years	56.4	~ 65.0[1,2]
Male sex, %	50.0	~ 70.0[1,2]
Predominant donor type	Related	Related[9,11,12,14]
Predominant graft source	PBSC	PBSC[9,11,12,14]
Predominant conditioning	RIC (BU/FLU)	RIC[9,11,12,14,15]
Exposure to hypomethylating agents, %	14.3	38.0[1]
HSCT performed, %	28.6	10.0-20.0[1,2]
Neutrophil engraftment, days	17.3	14.0-21.0[9,11,12,14]
Platelet engraftment, days	Not consistently available	Not uniformly reported
Formal prognostic model	Not consistently applicable	CPSS/CPSS-Mol/Mayo[1,2,9,11,12,14]

Values in the comparator column are representative benchmarks extracted from selected contemporary publications and are presented for descriptive contextualization only; they do not represent pooled meta-analytic averages. CPSS: CMML-specific Prognostic Scoring System. Source: Elaborated by the authors.

Descriptive comparison with the Latin American registry benchmark[10] also suggested similar early neutrophil engraftment despite demographic differences (Table 3).

Table 3. Latin American transplant registry benchmark vs. university hospital data.

Variable	Latin American registry benchmark	University hospital
Mean age, years	50.40	36.75
Male sex, %	90	50
Neutrophil engraftment, days	18	17

This registry comparison is descriptive and should be interpreted as a regional benchmark rather than a disease-matched external control; comparator values were obtained from the Latin American Bone Marrow Transplant Registry and related published context.[10] Source: Elaborated by the authors.

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DISCUSSION

The present single-center series provides a real-world view of CMML care in Northeastern Brazil and highlights the tension between modern disease management and the resource constraints of the public healthcare system. Although the study was not designed to formally measure diagnostic delay, the institutional absence of consistent molecular and cytogenetic risk assessment in most cases indicates restricted access to contemporary diagnostic and prognostic tools. This limitation is especially relevant in CMML, in which accurate classification and risk stratification depend on integrating clinical, morphologic, cytogenetic, and molecular data.[2-7]

Our cohort also illustrates restricted access to therapy. Only 14.3% of patients received hypomethylating agents, a figure far below that reported in large contemporary real-world cohorts.[1,8] In practical terms, this low exposure likely narrows the therapeutic window for patients who are not immediate transplant candidates and may contribute to progression before definitive referral. Because our retrospective dataset did not capture all drug-access pathways in a standardized manner, this finding should be interpreted as a signal of limited treatment access rather than a direct causal demonstration.

Median OS in the overall cohort was 25 months, similar to that of an international series of intermediate- or high-risk patients, where median survival generally ranges between 16 and 31 months.[2,11] Patients presenting in the acute phase had numerically worse survival than those diagnosed in the chronic phase, but statistical significance was not reached. This result is clinically plausible and consistent with transplant literature showing poorer outcomes when HSCT is delayed until blast transformation.[9,11,14,15]

The transplant journey itself appears to be shaped by both biological and non-biological barriers. In our cohort, transplanted patients had longer median OS than non-transplanted patients (25 vs. 8 months), although the comparison was exploratory and underpowered. Still, the direction of effect is coherent with broader evidence supporting HSCT as the only curative strategy in selected CMML patients.[9,11-15] The low socioeconomic profile often seen in the public system may further complicate optimization before HSCT by affecting nutrition, adherence, timely testing, and access to multidisciplinary support; however, these social determinants were not prospectively measured in the present study and should therefore be considered contextual rather than directly tested variables.

The clinical characteristics of our cohort differ from those of the published literature. Our patients were younger and had lower exposure to hypomethylating agents, yet transplant practice was broadly similar to that described in other CMML transplant series, with related donors, peripheral blood stem cells (PBSC) as the graft source, and RIC predominating.[9,11,12,14,15] These findings show that, despite clinical differences, early transplant outcomes are comparable to those of major international registries, at least with regard to neutrophil engraftment and short-term survival landmarks.[9,11,12,14]

Study limitations

This study has important limitations. It was retrospective, single-center, and based on a small sample, which restricts statistical power and precludes definitive causal inference. Several historical records lacked complete molecular, cytogenetic, and treatment-detail fields, limiting the formal application of prognostic models and preventing uniform recovery of variables such as age range, platelet engraftment time, and systematically codified non-HMA disease-directed therapy. In addition, external comparisons with the literature and registry data were descriptive rather than matched or pooled analyses. These limitations should be weighed when interpreting the survival differences observed between subgroups.

CONCLUSION

Ten years of follow-up of CMML patients in a public hospital in Northeastern Brazil reveal how structural, diagnostic, and therapeutic barriers shape the patient journey from diagnosis to transplantation. Limited

access to modern prognostic tools and disease-modifying therapy constrains risk stratification and treatment planning, while transplant eligibility and timing appear to be influenced by both clinical complexity and health-system barriers. Despite these challenges, patients who reached HSCT showed survival comparable to that of international registries, reinforcing that timely transplant care can improve CMML prognosis in the Brazilian public healthcare system.

CONFLICTS OF INTEREST

Nothing to declare.

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

Artificial intelligence tools were used to support language editing and drafting of parts of the manuscript. All content was reviewed, revised, and approved by the authors, who take full responsibility for the final version.

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DATA AVAILABILITY STATEMENT

Data will be provided upon request.

AUTHOR CONTRIBUTIONS

Conceptualization: Vasconcelos ETMFS, Duarte FB. **Investigation:** Vasconcelos ETMFS, Cunha FM, Oliveira GM, Rocha MLFC. **Methodology:** Vasconcelos ETMFS. **Formal Analysis:** Mota Segundo HA. **Data Curation:** Mota Segundo HA, Vasconcelos ETMFS. **Project Administration:** Vasconcelos ETMFS. **Funding Acquisition:** Not applicable. **Writing – original draft:** Vasconcelos ETMFS. **Writing – review & editing:** Vasconcelos ETMFS, Duarte FB. **Supervision:** Duarte FB. **Final Approval:** Vasconcelos ETMFS.

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