Essential Thrombocythemia in Colombia: A Real-World Single-Center Study

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Abstract

Myeloproliferative neoplasms are clonal hematologic disorders driven by recurrent somatic mutations; essential thrombocythemia (ET) is a classical entity within this group, although relatively uncommon. Molecular profiling refines both diagnosis and risk stratification.

This study describes an adult ET cohort treated at a comprehensive cancer center in Cali, Colombia. Patients diagnosed between July 2015 and July 2023 were retrospectively identified. Demographic, clinical, laboratory, molecular, therapeutic, and follow-up data were extracted from medical records. Risk was assigned according to established classification systems.

A total of 169 patients met diagnostic criteria. Median age at diagnosis was 68.3 years (range, 34–84), with female predominance. JAK2 V617F was detected in 59/169 patients (34.9%; 52.2% of those tested), and CALR mutations in 13/169 (7.7%; 54.2% of those tested); no MPL mutations were identified among the 13 patients tested. Mean platelet count at presentation was 886 × 10^9/L, and 58% of patients were classified as high thrombotic risk, primarily due to age >60 years and/or prior thrombosis.

Twenty-eight percent of cases were diagnosed incidentally; vasomotor and constitutional symptoms predominated among symptomatic patients. Initial management consisted of low-dose acetylsalicylic acid in low-risk patients and cytoreductive therapy (predominantly hydroxyurea), in high-risk individuals. During follow-up, thrombotic events occurred in 18.6% and hemorrhagic complications in 6.8%. Progression to myelofibrosis was documented in two patients; no leukemic transformation was observed.

This regional experience demonstrates overall concordance with international data while highlighting the high proportion of high-risk disease at diagnosis and limited molecular testing availability. These findings support timely molecular evaluation, risk-adapted therapy, and expanded access to diagnostic resources in Latin America.

Key words:

Thrombocythemia, Essential;
Hydroxyurea;
Janus Kinase 2;
Thrombosis;
Myeloproliferative Disorders.

Trombocitemia esencial en Colombia: Un estudio de un solo centro en condiciones reales

Resumen

Las neoplasias mieloproliferativas son trastornos hematológicos clonales impulsados por mutaciones somáticas recurrentes. La trombocitemia esencial (TE) es una entidad clásica dentro de este grupo, aunque relativamente infrecuente. El perfil molecular ha refinado tanto el diagnóstico como la estratificación del riesgo.

Se identificaron retrospectivamente pacientes diagnosticados entre julio de 2015 y julio de 2023 en un centro oncológico integral en Cali, Colombia. Se recolectaron datos demográficos, clínicos, de laboratorio, moleculares, terapéuticos y de seguimiento. La estratificación de riesgo se realizó según esquemas establecidos.

Un total de 169 pacientes cumplieron criterios diagnósticos. La mediana de edad al diagnóstico fue de 68,3 años (rango, 34–84), con predominio femenino. JAK2 V617F se detectó en 59/169 pacientes (34,9%; 52,2% de los evaluados), y mutaciones en CALR en 13/169 (7,7%; 54,2% de los evaluados); no se identificaron mutaciones en MPL entre los 13 pacientes analizados. El recuento medio de plaquetas al diagnóstico fue de 886 $\times$ 10^9/L, y el 58% se clasificó como de alto riesgo trombótico.

El 28% de los casos fue diagnosticado de manera incidental; entre los pacientes sintomáticos predominaron los síntomas vasomotores y constitucionales. El manejo inicial consistió en ácido acetilsalicílico a dosis bajas en pacientes de bajo riesgo y terapia citorreductora (principalmente hidroxiurea) en pacientes de alto riesgo. Durante el seguimiento, los eventos trombóticos ocurrieron en el 18,6% y las complicaciones hemorrágicas en el 6,8%. Se documentó progresión a mielofibrosis en dos pacientes y no se observaron transformaciones leucémicas.

Esta experiencia regional demuestra concordancia con series internacionales y resalta la alta proporción de enfermedad de alto riesgo al diagnóstico, así como las limitaciones en el acceso a estudios moleculares. Los hallazgos apoyan la evaluación molecular oportuna, el tratamiento adaptado al riesgo y la ampliación del acceso diagnóstico en América Latina.

Palabras clave:

Trombocitemia Esencial;

Hidroxiurea;

Janus Quinasa 2;

Trombosis;

Trastornos Mieloproliferativos.

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Introduction

Myeloproliferative neoplasms (MPNs) are a heterogeneous group of clonal hematologic malignancies characterized by dysregulated proliferation of one or more myeloid lineages. These disorders result from acquired somatic mutations in hematopoietic stem cells, leading to constitutive activation of signaling pathways that promote cellular proliferation and survival (1). The classic BCR-ABL1–negative MPNs include essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF), whereas chronic myeloid leukemia (CML) is defined by the presence of the BCR-ABL1 fusion gene (2,3).

Essential thrombocythemia is a neoplasm that arises from the uncontrolled proliferation of a myeloid progenitor committed to the megakaryocytic lineage, generating a drastically increased concentration of platelets in the peripheral blood. Most cases of ET are caused by mutations in the JAK2 gene, specifically the V617F mutation in which there is a single nucleotide change of G to T in codon 617, in exon 14 in nucleotide 1849, resulting in a change of valine to phenylalanine. Other cases might underlie mutations in JAK2 exon 12, CALR or MPL (4-7). Clinically, ET is characterized by isolated thrombocytosis, sometimes accompanied by mild or moderate leukocytosis. Due to this dysregulated thrombocyte growth, common symptoms include fatigue, headache, pruritus, thrombotic events and even hemorrhage(8).

There is a lack of understanding of ET in the Hispanic population from Latin American countries. In Colombia, Giraldo-Rincón et al. published a cross-sectional study reporting the mutational frequencies in the JAK2, CALR and MPL in 53 patients with BCR-ABL1-negative MPNs, however, this manuscript was not focused on ET and there were no data regarding evolution of the disease and survival outcomes (9). Similarly, Abello et al. described demographic and hematologic characteristics from a multicenter Colombian cohort that included 93 patients with ET, but without detailed analysis of clinical course or survival (10).

To our knowledge, the present study represents the largest single-center cohort of Colombian patients with essential thrombocythemia, providing comprehensive data on clinical characteristics, mutational profile, management strategies, and outcomes over an eight-year period.

Methods

Study design: a retrospective cohort study was conducted including patients with a diagnosis of essential thrombocythemia (ET) treated at a specialized outpatient oncology center in Colombia. The observation period spanned from July 2015 through July 2023. Diagnosis and clinical management followed the World Health Organization (WHO) criteria in effect at the time of diagnosis; confirmatory documentation by the treating hematologist was required for inclusion.

Sample and data collection: consecutive sampling of electronic medical records was used. The sample included all consecutive patients evaluated during the study period who had a diagnosis of essential thrombocythemia (ET) at an outpatient center specialized in oncology care. Following institutional approval, clinical records identified through predefined ICD-10 codes consistent with essential thrombocythemia were reviewed using anonymized databases. An anonymized analytic dataset was created using a structured data abstraction form and standardized codebook, including the following variables:

- **Demographics:** sex; age at **symptom onset** and at **diagnosis**.
- **Genetics: JAK2, CALR and MPL** mutation status.

  Molecular testing was not systematically available for all patients due to the retrospective design and evolving diagnostic practices over the study period. JAK2 V617F testing was performed in 113/169 patients (66.9%), CALR mutation analysis in 24/169 (14.2%), and MPL mutation analysis in 13/169 (7.7%). Mutation frequencies are therefore reported both as percentages of tested patients and of the overall cohort.
- **Laboratory: platelet count** at baseline and at end of follow-up (or last available visit within the window).
- **Therapy and course: initial management** (e.g., antiplatelet and/or cytoreductive therapy), **relapse** during follow-up (as documented by the treating hematologist), and **risk stratification** at diagnosis **as recorded in clinical** notes (e.g., conventional or IPSET-Thrombosis–based categories, when available).

Operational definitions: "Relapse" was defined as **physician-documented disease progression or recurrence** requiring a change in management and/or meeting laboratory/clinical thresholds prompting therapeutic modification. Where multiple platelet measurements were available, baseline was defined as the closest value to and within **±30 days** of diagnosis.

Data quality: to minimize information bias, two trained abstractors performed **double data entry** on a 10% random sample; discrepancies were resolved

by consensus with a senior hematologist. Range checks and internal consistency rules (e.g., date sequences, physiological limits) were applied before database lock.

Statistical analysis: statistical analyses were conducted in R using two-sided tests with a significance level of $\alpha = 0.05$. Continuous variables were summarized as mean ± standard deviation or median (interquartile range) according to distribution assessed by the Shapiro–Wilk test. Categorical variables were described as counts and percentages.

Group comparisons between deceased and surviving patients were performed using Student's t test or Mann–Whitney U test for continuous variables, and χ^2 test or Fisher's exact test for categorical variables, as appropriate. All analyses were exploratory and unadjusted.

Results

A total of 169 patients with essential thrombocythemia were included. Most participants were female (60.9%). The median age at diagnosis was 68.3 years. The mean age at symptom onset was 58.7 ± 13.7 years, with a mean interval of 7.2 ± 19.4 months between symptom onset and diagnosis. Regarding molecular profiling, JAK2 V617F mutation was identified in 59/113 tested patients (52.2%), corresponding to 59/169 (34.9%) of the overall cohort. CALR mutations were detected in 13/24 tested patients (54.2%), representing 13/169 (7.7%) of the total population. No MPL mutations were identified among the 13 tested patients. Additionally, 58.0% of patients were classified as high risk at diagnosis (**Table I**).

The mean baseline platelet count was 886 ± 415 × 10^9/L. The most frequently prescribed initial regimen was hydroxyurea combined with aspirin (49.7%). This management strategy was associated with a reduction in platelet counts, with a final mean value of 583 ± 273 × 10^9/L. During follow-up, 21.3% (approximately one-fifth) of patients died (Table I).

Regarding clinical presentation, 28.0% of cases were diagnosed incidentally. During the follow-up period, thrombotic events occurred in 18.6% of patients, while hemorrhagic complications were documented in 6.8%.

Outcome-related factors

A higher proportion of deaths occurred among men (30.3%; p = 0.022). Patients who died were significantly older at diagnosis (mean 81.6 ± 9.4 years; p = 0.006). Additionally, the interval between symptom onset and diagnosis was longer among deceased patients (12.5 ± 26.3 months; p = 0.002).

The high-risk group exhibited a greater proportion of deaths (26.5%; p = 0.022) (**Table II**).

Regarding hematologic parameters, deceased patients had higher mean platelet counts both at baseline (960 ± 455 × 10^9/L; p = 0.047) and at last follow-up (667 ± 400 × 10^9/L; p < 0.001). Treatment with hydroxyurea monotherapy was significantly more frequent among patients who died (33.9%; p = 0.022) (**Table II**).

Table I. Clinical and demographic characteristics of patients with essential thrombocythemia (ET) (n = 169).

		n	%
Demographic characteristics			
Sex	Female Male	103 66	60.90% 39.10%
Age (years)	(Mean ± SD)	68.3	14.8
Clinical characteristics			
Age at symptoms onset Age at diagnosis Time to diagnosis (months) JAK2 mutations	(Mean ± SD) (Mean ± SD) Median (IQR) Unknown Negative Positive	58.7 68.3 7.2 56 54 59	13.7 14.8 19.4 33.10% 32.00% 34.90%

CALR mutations	Unknown	145	85.80%
	Negative	11	6.50%
	Positive	13	7.70%
MPL mutations	Unknown	156	92.30%
	Negative	13	7.70%
	Positive	0	0%
Risk of thrombosis	High	98	58.00%
	Intermediate	33	19.50%
	Low	38	22.50%
Management and follow-up			
Baseline platelets ($\times 10^9$/L)	(Mean ± SD)	886.7	415.0
First-line therapy	ASA	17	10.10%
	Hydroxyurea	59	34.90%
	Hydroxyurea + ASA	84	49.70%
	NA	9	5.30%
Last follow-up platelets ($\times 10^9$/L)	(Mean ± SD)	583.3	272.6
Outcome	Dead	36	21.30%
	Alive	133	78.70%

Abbreviations: ASA, Acetylsalicylic acid. Source: Author's own elaboration.

Tabla II. Characteristics related to outcomes in patients with ET

		Outcome				
		Dead		Alive		P value
		n	%	n	%	
Demographic characteristics						
Sex	Female	16	15.50%	87	84.50%	0.022
	Male	20	30.30%	46	69.710%	
Age (years)	(Mean ± SD)	81.6		64.8	13.9	0.006
Clinical characteristics						
Age at symptoms onset	(Mean ± SD)	69.2	10.6	56.3	13.2	0.152
Age at diagnosis	(Mean ± SD)	70.2	9.2	56.5	13.8	0.012
Time to diagnosis (months)	Median (IQR)	12.5	26.3	6	17.3	0.002
JAK2 mutations	Unknown	19	33.90%	37	66.10%	0.001
	Negative	3	5.60%	51	94.40%	
	Positive	14	23.70%	45	76.30%	
CALR mutations	Unknown	34	23.40%	111	76.60%	0.161
	Negative	0	0.00%	11	100.0%	
	Positive	2	15.40%	11	84.60%	
MPL mutations	Unknown	36	23.10%	120	76.90%	0.051
	Negative	0	0.00%	13	100.0%	
	Positive	0	0.00%	0	100.0%	
Risk of thrombosis	High	26	26.50%	72	73.50%	0.022
	Intermediate	8	24.20%	25	75.80%	
	Low	2	5.30%	36	94.70%	
Management and follow-up						

Baseline platelets (×10⁹/L)	(Mean ± SD)	960.2	455.2	866.5	402.7	0.047
First-line therapy	ASA	1	5.90%	16	94.10%	0.012
	Hydroxyurea	20	33.90%	39	66.10%	
	Hydroxyurea + ASA	14	16.70%	70	83.30%	
	NA	1	11.10%	8	88.90%	
Last follow-up platelets (×10⁹/L)	(Mean ± SD)	667.4	400.0	560.4	222.5	<0.001

Abbreviations: ASA, acetylsalicylic acid; NA, Not applicable.Source: Author's own elaboration.

Discussion

To the best of current knowledge, this cohort represents the largest single-center description of essential thrombocythemia (ET) in Colombia, providing valuable epidemiologic and clinical insights into this rare myeloproliferative neoplasm. The median age at diagnosis (68.3 years) is consistent with the natural history of ET described in well-characterized populations such as Europe and North America, where diagnoses typically occur during the sixth to seventh decades of life (7,11).

The observed female predominance (60.9%) is consistent with international cohorts, where essential thrombocythemia typically shows a higher prevalence in women.

Molecular characterization revealed JAK2 V617F in 34.9% of cases and CALR mutations in 7.7%, with a large proportion of cases lacking molecular characterization. These frequencies are lower than those reported in large European and U.S. registries, where JAK2 mutations occur in 50–60% and CALR in 20–25% of patients (12,13). It is important to emphasize that these percentages were calculated based on the total study population (n=169); the high proportion of patients with unknown molecular status significantly influences these figures and likely leads to an underestimation of the true mutational prevalence in our setting. The underrepresentation of CALR and MPL mutations in this series likely reflects limitations in molecular testing availability during much of the study period, highlighting a persistent diagnostic gap in resource-constrained settings. Expanding access to next-generation sequencing or targeted PCR panels is critical for improving diagnostic precision and refining risk stratification (14,15).

Therapeutic management was largely aligned with international standards, with hydroxyurea (alone or in combination with aspirin) being the predominant first-line cytoreductive therapy(15). Treatment with hydroxyurea monotherapy was significantly more frequent among patients who died (representing 33.9% of this subgroup), whereas combination therapy with hydroxyurea and aspirin was the predominant strategy overall and was associated with better survival. While the study design precludes causal inference, these findings raise important questions regarding treatment optimization in high-risk patients and suggest that dual therapy may confer additional protection in similar clinical populations.

Overall mortality was 21.3% and was associated with advanced age, longer interval from symptom onset to diagnosis, high-risk classification, and persistently elevated platelet counts. While causal relationships cannot be established, these observations suggest that delayed recognition of ET may contribute to adverse outcomes. ET remains under-recognized in primary care settings, where thrombocytosis is frequently attributed to reactive etiologies (16,17). Educational initiatives for physicians and systematic referral pathways to hematology could mitigate diagnostic delays and improve outcomes.

Compared to global benchmarks, the high-risk proportion (58%) in our cohort is notable. This may be partly due to referral bias to a tertiary cancer center, where patients tend to present with more advanced or complicated disease. Nonetheless, it highlights the clinical burden ET imposes on our region and the need for early identification and risk-adapted management strategies(7,15).

Limitations

This study has inherent limitations. Its retrospective design is subject to missing data, particularly regarding molecular status and long-term outcomes such as thrombotic or hemorrhagic events. Mortality attribution could not be fully adjudicated, limiting the ability to distinguish

essential thrombocythemia–related deaths from unrelated causes. Additionally, as a single-center cohort, generalizability to the broader Colombian or Latin American population should be approached with caution. Nonetheless, the relatively large sample size and systematic follow-up strengthen the internal validity of the findings and provide a foundation for future prospective, multicenter collaborations.

Conclusions

This study provides the first large-scale characterization of essential thrombocythemia in a Colombian population. Patients were predominantly older adults, with a female predominance, and more than half were classified as high risk. Molecular profiling was limited, with lower rates of JAK2 and CALR mutations than expected, reflecting diagnostic gaps in resource-constrained settings. Mortality was associated with advanced age, longer interval to diagnosis, higher platelet counts, high-risk classification, and hydroxyurea monotherapy in unadjusted analyses, underscoring the importance of timely referral, comprehensive risk stratification, and optimization of therapy.

These findings reinforce the urgent need to expand molecular diagnostics, standardize risk-adapted management, and promote earlier detection of ET in Colombia. Future multicenter, prospective studies across Latin America are warranted to validate these observations, identify regional differences, and guide tailored strategies to improve patient outcomes(7,15,17).

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Conflicts of interest

The authors declare that they have no conflicts of interest related to this work.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions (CRediT)

HANC, LVAC, RGG: Conceptualization

HANC, LVAC, MAUB, WOE, MAO, MCL: Methodology

HANC, MAUB: Formal analysis

HANC, LVAC, ILP: Writing – original draft

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Justification of authorship: The number of authors is justified by the nature of this real-world observational study, which required distinct phases including methodological design, systematic data collection and curation of clinical records, formal analysis, validation of results, and specialized supervision in hemato-oncology. Each author contributed substantially to at least one key aspect of the research process, in accordance with international authorship criteria.

Use of Artificial Intelligence

The authors declare that generative artificial intelligence (Google Gemini) was used exclusively for language editing and technical translation in specific sections of the manuscript. No AI tools were used for data analysis, interpretation of results, or generation of scientific content. The authors assume full responsibility for the accuracy, integrity, and originality of the work.

Publication statement

This manuscript has not been previously published, nor is it under consideration for publication elsewhere. It has not been submitted to any other journal, conference, or academic platform.

Ethical considerations

The study was conducted in accordance with the ethical principles of biomedical research, Good Clinical Practice guidelines, and the principles of the Declaration of Helsinki. The study protocol was reviewed and approved by the Research Ethics Committee CAIMED of the IDC Instituto de Cáncer Hemato Oncólogos, Cali, Colombia (Approval No. 235; approval date: 18/07/2024).

Given the retrospective and low-risk nature of the study, the requirement for informed consent was waived by the ethics committee. Data confidentiality and protection were ensured at all times in accordance with applicable regulations.

Transparency statement

The corresponding author confirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained.

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