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ORIGINAL ARTICLE

Prevalence and Clinical Significance of FLT3 Mutation Status in Acute Myeloid Leukemia Patients: A Multicenter Study

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Background and Aims. FLT3-ITD mutations in acute myeloid leukemia (AML) are associated with a poor prognosis. In Latin America, little epidemiological data exist about these mutations and their influence on clinical evolution and prognosis. Standardization and well-established clinical correlation make FLT3 mutational analysis by molecular methods an invaluable tool to decide among treatment options and to determine AML prognosis.

Methods. We assessed the prevalence of FLT3-ITD mutations in 138 patients with AML at four hematology referral centers from Mexico and Colombia. Molecular methods based on polymerase chain reaction (PCR) were employed for determining FLT3-ITD status.

Results. Mutations were present in 28 patients indicating a prevalence of 20.28%. Median age was 47 years (5–96). The FLT3 mutation positive group was older, had higher WBC and hemoglobin values and lower platelet counts but without statistical significance. A not previously described mutation in the FLT3 gene was found in one patient involving a nucleotide exchange of timine for cytosine at the 66608 position. A high mortality was found in the FLT3-mutated group, 67.8 vs. 42.72% in the non-mutated group and median survival was 4.9 months vs. 20.4 months, $p = 0.009$. A mutated FLT3 did not confer poor prognosis to those with M3 AML. The mutated FLT3 population had poor overall survival (OS) despite hematoprogenitor stem cell transplantation (HSCT).

Conclusion. Prevalence of FLT3-ITD mutation in AML was present in a proportion comparable to other populations and, when present, was associated with a very poor prognosis.

Key Words: Acute myeloid leukemia, AML, FLT3, Latin America.

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Introduction

FLT3 is a tyrosine kinase receptor with an important role in survival and proliferation of hematopoietic stem cells. This receptor is mutated in about one third of acute myeloid leukemia (AML) patients, either by internal tandem duplication (ITD) of the juxta-membrane domain or by point mutations involving the kinase domain (KD); both mutations constitutively activate FLT3 (1). Most studies suggest that the ITD/FLT3 mutation is associated with a poor prognosis due to a major relapse rate and minor overall survival (2−10). Therefore, molecules have been developed that block tyrosine kinase specifically against FLT3 with some encouraging results (11). AML patients who have no FLT3 mutations at diagnosis can present these later during the course of the disease, generally during relapse.

When FLT3 mutations combine with other genetic alterations, complete transformation to AML occurs. Most patients receiving FLT3 inhibitors have a short duration of response, with peripheral blood blasts reappearing after weeks or months, leading to a high mortality rate (12−14). In Latin America there are few epidemiological data regarding the frequency and impact on clinical outcome of the FLT3 mutation (15−21). Arana-Trejo (16) found an ITD/FLT3 mutation prevalence of 15% in Mexico City population. Lucena-Araujo et al. (15) in Brazil found ITD/FLT3 in 23.6%, with lower OS for patients with ITD/FLT3 (5.8 months vs. 25.8 months, 95% CI: 13.5−38, $p = 0.004$).

A second FLT3 mutation involves aspartic acid 835 of the kinase domain (KD). Its incidence is significantly low and its prognostic value has not been completely determined. Some studies have shown that the survival of patients with the kinase domain mutation (KD) at diagnosis is greater (22). Therefore, it is important to describe the characteristics and clinical behavior of patients with AML who exhibit FLT3 mutations to determine similarities and differences with other populations. The present study determined the prevalence of FLT3 in patients with AML in three Mexican centers and one Colombian center.

Materials and Methods

Patients

Patients diagnosed with de novo or secondary AML established by morphological examination and flow cytometry of blood or bone marrow samples and in whom FLT3 mutational status was determined between 2010 and 2014 were studied. We included 138 samples of patients attending the Hematology Service of the Internal Medicine Department, ''Dr. José Eleuterio González'' University Hospital of the School of Medicine of the Autonomous University of Nuevo Leon (UANL) in Monterrey, the Hematology Service of the Hospital General in Mexico City, the Clínica Ruiz of Puebla, México and the Genetic Service of the University of Antioquia, Medellin, Colombia. AML was diagnosed using morphology criteria according to the FAB classification (23), by immunohistochemical staining and/or by immunophenotype profile according to institutional guidelines. A peripheral blood sample was drawn or a bone marrow sample was obtained by aspiration. Patients were cytogenetically classified into three risk groups: favorable, intermediate, and adverse (24−27).

Treatment

Patients received treatment based on a previous report (13). Induction to remission therapy consisted of doxorubicin, 40 mg/m^2 or mitoxantrone 10 mg/m^2 on days 1−3 and cytarabine 100 mg/m^2 (by continuous intravenous infusion every 24 h) on days 1−7. Intrathecal chemotherapy consisted of methotrexate 15 mg, cytarabine 30 mg and dexamethasone 4 mg, delivered at the beginning of each cycle of therapy. Bone marrow aspiration was performed on day 21. Induction to remission was followed by intensification consisting of intrathecal chemotherapy and intravenous chemotherapy with cytarabine at 3 g/m^2 delivered by a 4 h infusion on days 1−4 and etoposide at 150 mg/m^2/day in a 2 h infusion on days 1−3. Recovery, including neutrophils $>1.0 \times 10^9$/l and platelets $>100 \times 10^9$/l, was followed by two additional cycles of intensification as described above. With respect to standard care, patients received prophylaxis with trimethoprim-sulfamethoxazole and itraconazole during the stages of post-chemotherapy neutropenia. Patients with febrile neutropenia were hospitalized, initiating treatment with a carbapenem (imipenem or meropenem) combined with vancomycin. According to the response to treatment, amphotericin was added in patients with persistent fever. Patients received red blood cell transfusion when hemoglobin was <8.0 g/dL and prophylactic platelet transfusion when the platelet count was $<20 \times 10^9$/L. Standard follow-up was carried-out daily during hospitalization periods and then weekly or monthly, according to clinical evolution. HSCT was performed if a donor was available. The local Ethics and Research Committees approved the protocol of the study.

Sample Processing

DNA was extracted from peripheral blood or from bone marrow with the automatic Maxwell® 16 System (Promega Corporation, Madison, WI) using the principle of cellular lyses and binding nucleic acids to magnetized silica particles. Later, the quality and DNA concentration was evaluated with the NanoDrop ND-1000 spectrophotometer (NanoDrop Technologies, Inc., Wilmington, DE). Once an optimal concentration and quality of DNA was obtained, ITD and KD mutations detection was performed with the

Table 1. Characteristics for 138 patients with acute myeloid leukemia at four Hematology Centers in México and Colombia in whom the FLT3 mutation was studied, there was no difference in prevalence among centers

	Global $n = 138$ (100%)	FLT3 (+) $n = 28$ (20.3%)	FLT3 (−) $n = 110$ (79.7%)	p
Age years (median, range)	41 (4–97)	47 (5–96)	39 (4–97)	0.06[a]
Gender				0.52
Female	73 (52.9)	13 (46.4)	60 (54.5)	
Male	65 (47.1)	15 (53.6)	50 (45.5)	
CBC (mean ± SD)				
Hemoglobin (g/dL)	8.8 (2.6)	9.3 (2.2)	8.6 (2.7)	0.14[a]
WBC (10^9/L)	5.84 (1.54)	6.60 (1.07)	5.64 (1.59)	0.20
Platelet (10^9/L)	88.4 (10.3)	72.6 (6.34)	92.5 (11.08)	<0.001
FAB Type				0.87+
M0	2 (1.5)	-	2 (1.8)	
M1	7 (5.1)	2 (7.1)	5 (4.6)	
M2	66 (47.5)	13 (46.4)	53 (48.1)	
M3	18 (13.0)	4 (14.3)	14 (12.8)	
M4	22 (16.0)	3 (10.7)	19 (17.3)	
M5	18 (13.0)	6 (21.5)	12 (10.9)	
M6	3 (2.1)	-	3 (2.7)	
M7	2 (1.5)	-	2 (1.8)	
Center				0.67+
Mexico City	30 (21.7)	8 (28.6)	22 (20.2)	
Monterrey	34 (24.6)	7 (25.0)	27 (24.5)	
Puebla	45 (32.6)	9 (32.1)	36 (32.7)	
Medellín	29 (21)	4 (14.3)	25 (22.7)	

[a]Student's t; + χ^2; WBC, white blood cell; t, translocation; inv, inversion; FLT3 (+), FLT3 mutated; CBC, complete blood count.

GeneAmp PCR System 9700 (Applied Biosystems, Foster City, CA) through amplification of exons 14, 15 and 20 with specific primers of FLT3 gen region using the Seeplex® FLT3 Genotyping kit (Seegene, Rockville, MD). Later, an electrophoretic analysis of the amplified products was done in 2% agar gel stained with ethidium bromide and observed by transillumination. PCR was performed using forward and reverse FLT3 primers (5′GCAATTTAGGTATGAAAGCCAGC′3 and 5′CTTT CAGCATTTTGACGGCAACC′3) amplifying a 329-bp product (normal) or a major band for patients with the IDT insertion. FLT3-ITD and FLT3-WT bands were cut and eluted from 2.5% agarose gel and purified with the QIAquick PCR Purification Kit (Qiagen, Valencia, CA) following the manufacturer's instructions. Purified DNAs were sequenced using Big Dye Terminator cycle sequencing chemistry (Applied Biosystems).

Statistical Analysis

Comparisons between groups were performed using χ^2/Fisher's exact test for categorical data and Student t test/Mann-Whitney U test for quantitative data. Cox regression analysis was performed to assess the impact of several variables on patient outcome. The Kaplan–Meier method was used for assessing OS, from the day of diagnosis until either the last follow-up or death and the log-rank test to evaluate differences between survival distributions with a 95% confidence interval (CI). Two-sided p values <0.05 were considered significant. All values were generated using IBM SPSS® (SPSS Inc., Chicago, IL) v.20.0 for Windows.

Results

Data of 138 patients diagnosed with AML were recorded. The global median age at diagnosis was 41 years (4–97 years); 52.9% were females ($n = 73$) and 47.1% males ($n = 65$). Median follow-up was 9.9 months (range 0.10–95.5). The most common variety was M2, which was present in 47.5% of patients; the M3 group accounted for 13% of cases ($n = 18$). General characteristics including complete blood count, FAB type and general distribution of patients are included in Table 1. Cytogenetic analysis results are shown in Table 2. Figure 1 shows the total number of patients per center and number of those with FLT3 mutation.

Mutational Analysis of FLT3 and Clinical Features

The FLT3 mutation was found in 28/138 cases for a prevalence of 20.3%; four had the KD mutation. Median age was 47 years (range 5–96 years). Patients with the mutation had higher median age than those without it (47 vs. 39 years, $p > 0.05$). A mutation was detected in 16.7% of the population <55 years of age and in 27.5% of older patients ($p = 0.16$), not shown. The most frequent

Table 2. Cytogenetic findings in 84 acute myeloid leukemia patients, 28 in the FTL-3 (+) and 56 in the FLT-3 (−) group

Cytogenetic	*n* = 84 (%)	*n* = 28 (%)	*n* = 56 (%)
Intermediate risk	*n* = 51 (60.7)	*n* = 16 (57.1)	*n* = 35 (62.5)
Normal	38 (45.2)	13 (46.3)	25 (44.6)
Trisomy 8	2 (2.4)	1 (3.6)	1 (1.8)
Deletion 9q	1 (1.2)	-	1 (1.8)
Polyploid cytogenetics	3 (3.6)	1 (3.6)	2 (3.6)
4q deletion	1 (1.2)	1 (3.6)	-
Others	6 (7.1)	-	6 (10.7)
Favorable risk			
t (15,17)	8 (9.5)	4 (14.3)	4 (7.1)
t (8,21)	10 (11.9)	-	10 (17.8)
Inv (16)	8 (9.5)	4 (14.3)	4 (7.1)
Unfavorable risk			
t (9,22)	1 (1.2)	-	1 (1.8)
t (;6;11)	4 (4.8)	4 (14.3)	-
Deletion 7	1 (1.2)	-	1 (1.8)
Inv (3)	1 (1.2)	-	1 (1.8)

FAB variety was M2 followed by the M5−M4 subtype. Blood cell counts (CBC) and AML morphological subtypes at diagnosis are described in Table 1. Eighty-five percent of cases with a FLT3 mutation had *de novo* AML. Only one patient with M2 AML and the FLT3 mutation had central nervous system (CNS) involvement. Two patients had disseminated intravascular coagulation (DIC), one with M3 and another with M5, who had a NPM1 mutation. Only one M2 patient had extramedullar compromise (skin). A total of 23/28 patients were evaluable for response to standard induction chemotherapy with a response rate of 78.3% (13 CR and 5 PR). Nineteen of 28 patients with the ITD/FLT3 mutation died, for a mortality rate of 67.8%. The FLT3 mutation rate was higher among patients with an intermediate risk by cytogenetics (62.5%) compared to those from the adverse risk group (12.5%) (data not shown). Patients with the mutation had higher median age than those without the mutation (47 vs. 39 years, $p > 0.05$).

Features of Patients without FLT3 Mutations

Patients lacking the FLT3 mutation had a median age of 39 years (4−97 years) at diagnosis. CBC characteristics and AML subtypes are shown in Table 1. Fifty-six patients (50.9%) had cytogenetic analysis. During their evolution, six patients had CNS involvement (five with M2 and one with M5 AML), five had extra medullar involvement, and seven had DIC (all M3). A total of 85/110 patients were evaluable for response to standard induction chemotherapy, with a 74.1% rate response (55 CR and 8 PR). Forty-seven of 110 patients without the FLT3 mutation died, with a mortality rate of 42.72%.

Survival

Global median survival was 12.5 months (CI 3.8−21.1), 4.9 months for patients with the FLT3 mutation vs. 20.4 months for those without the mutation ($p = 0.009$) (Figure 2). Because the cytogenetic intermediate risk group represented 62.5%, it was further analyzed by the log rank test, without finding a significant difference in OS between FLT3-negative and -positive patients ($p = 0.220$). No significant differences in survival were found in the group of patients >55 years of age in relation to the presence or absence of the mutation ($p = 0.32$). Younger patients (<55 years) had a higher mortality in the FLT3 positive group ($p = 0.023$). The presence or absence of the FLT3 mutation in patients with the morphologic subtype M3 did not impact mortality ($p = 0.28$) but did in non-M3 subtypes ($p = 0.017$).

The influence of clinical−biological characteristics and FLT3 expression in univariate analysis using Cox regression showed that variables that were significantly

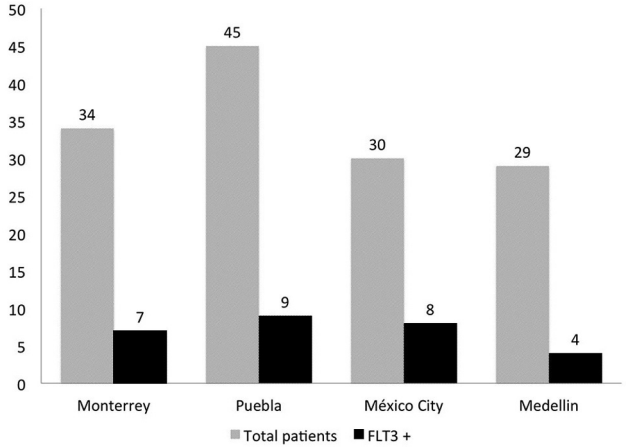

Figure 1. Number of cases of acute myeloid leukemia and of FLT3-mutated patients according to participant center.

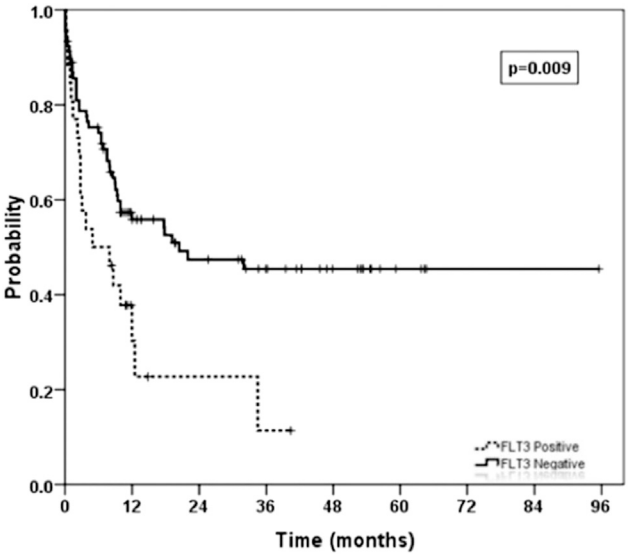

Figure 2. Overall survival of acute myeloid leukemia patients with and without the FLT-3 mutation.

Table 3. Salient basal features for 19 patients with acute myeloid leukemia treated with hematopoietic stem cell transplantation

	Global $n = 19$ (%)	FLT3 (+) $n = 4$ (%)	FLT3 (−) $n = 15$ (%)
Age (median)	35 (5–86)	26 (5–86)	35 (9–86)
Gender (M/F)	10/9	4/0	6/9
WBC (mean)	37053	43250	35401
Hb (mean)	11.85	10.62	11.85
Platelet (mean)	128053	87250	138933
Cytogenetics			
Normal	0	0	0
Molecular			
NPM1 mutated	1 (5.3)	1 (50)	0
CNS involvement	1 (5.3)	1 (50)	0
BMA at day 21			
CR	13 (68.4)	2 (50)	11 (73.3)
PR	5 (26.3)	2 (50)	3 (20)
NE	1 (5.3)	0	1 (6.7)
HSCT type			
Allogeneic	17 (89.5)	3 (75)	14 (93.3)
Autologous	2 (10.5)	1 (25)	1 (6.7)
Survival probability (median, mo)	32 (95%CI, 16.2–47.8)	5 (95% CI, 0.0001–12.8)	36 (95% CI, 25.3–46.7)
Status			
Alive	9 (47.4)	1 (25%)	8 (53.3)
Dead	10 (52.6)	3 (75%)	7 (46.7)

CR, complete response; PR, partial response; NE, not evaluable; CNS, central nervous system; HSCT, hematopoietic stem cell transplantation; BMA, bone marrow aspiration.

associated with decreased OS were low hemoglobin ($p = 0.02$) and FLT3 status ($p = 0.011$). In multivariate Cox regression analysis a higher hemoglobin level was a significant prognostic factor, with a hazard ratio (HR) of 0.874 (CI 0.867–0.968) $p = 0.008$, as well as FLT3 status, with a HR of 2.21 7 (CI 1.253–3.922) $p = 0.006$ (data not shown).

Hematopoietic Stem Cell Transplantation

Nineteen patients received a HSCT, four had FLT3 mutations and 15 did not. Characteristics for these patients are shown in Table 3. The FLT3 mutated population had a lower median survival probability compared with the non-mutated population (5 vs. 36 months, $p = 0.0001$).

Molecular Findings in FLT3 Mutations

In the two bands amplified in Colombian patients with ITD FLT3 mutation, all sequences corresponded to the normal allele of the juxtamembrane domain. In one Colombian patient, one cloned and sequenced colony showed a nucleotide exchange of timine by cytosine at 66608 position of FLT3 gene. This mutation has not been previously reported. This nucleotide change causes valine to be replaced by histidine in position 615 at the juxtamembrane domain of the FLT3 receptor. With respect to the size of the ITD FLT3 in the Mexican population, all ITDs had a <100 bp (mean of 60 bp) size and analysis revealed that in all of the six sequenced samples the beginning of the insertion was located in the 5′ of exon 14 and part of the intron, whereas the initial part of exon 15 in all patients was normal. Among the six AML patients analyzed, only one showed a clear sequence of the insertion of 82 bp. The remaining samples had mosaicism and the sequence of the insert could not be accurately detected.

Discussion

We previously showed that the median age of AML patients in México is ~32 years (28); therefore, it is not surprising that this study included a relatively young population (median age 41 years). The presence of the FLT3 mutation was documented in 20.3% with a direct negative impact on overall survival, which is similar to what has been previously described (29–31). Despite the development of various drugs directed at specific molecular targets, AML continues to have a high morbidity and mortality rate with early relapses. The different prognostic indexes in AML, including age and cytogenetics, help to identify patients with a high risk of relapse or refractory disease (23–27). The ITD/FLT3 mutations have been related with a dismal outcome in both adult and pediatric populations with AML and have acquired a critical role in treatment decisions (3,6,9,10). In Latin America, there are few statistics on the prevalence of ITD/FLT3 and its clinical significance. In a Brazilian patient series, Lucena-Araujo et al. (15) observed an ITD/FLT3 prevalence of 23.6%. Other Latin American groups reported ITD/FLT3 mutation prevalence with variable results: Mexico City 15%, Costa Rica 14.3% (pediatric population), Colombia 9.4%, and Argentina 16.7% (16–19,21) (Table 4).

Table 4. Data of FLT3 mutation prevalence surveys in Latin America

Country/Reference	Brazil (15)	Argentina Univ. Nacional de Córdova (18)	Monterrey-Mexico City-Puebla-Colombia
Patients (*n*)	169	36	138
Centers	1	1	4
FLT3 Prevalence	23.6% (40/169)	16.7% (6/36)	20.28% (28/138)
Hemoglobin at diagnosis $\times 10^3/mm^3$ (mean)	8.6		9.3
WBC at diagnosis $\times 10^3/mm^3$ (mean)	54		66
Platelet at diagnosis $\times 10^3/mm^3$ (mean)	38		72.6
Age (median in years)	46.6 (17−91)	47 (28−65)	47 (5−96)
Normal cytogenetic	11 (27.5%)		12 (42.9%)
Follow-up (median in months)	64.7 (28.6−88.8)		6.4 (0.20−40.4)
Overall survival (median in months)	5.8 (95% CI 0.98−10.7		4.9 (95% CI 0−11.7)
TKD/FLT3 (+)	1 (0.6%)	0	4 (2.9%)
Sex M:F	16:24	3:3	15:13
Subtype M4/M5		4/6 (66%)	9/28 (32%)
Subtype M3		1 (16%)	4/28 (14%)
Subtype M1/M2		1 (16%)	15/28 (53%)

Interestingly, most (46.4%) of the mutations in our study were detected in patients from the M2 FAB morphology group, which contrasts with previous reports where M2 had a significantly lower prevalence in relation to other FAB groups (32). Also, in our study population, patients with the FLT3 mutation had a higher median WBC at diagnosis compared to those without the mutation, but the difference was not significant and had no impact on OS after multivariate analysis. Despite the constant presence of this trend, there are few studies that yield statistical significance in this aspect. ITD/FLT3 mutations are identified in nearly 35−45% of patients with normal cytogenetics (33−35). In the present study we found the ITD/FLT3 mutation in 44% of 16 patients with normal cytogenetics, for a similar prevalence to that reported in the literature. It is noteworthy to underscore that cytogenetics has limitations in the Latin American population because there is no standardization of techniques and resources are limited.

Similar to that reported previously where the presence of the mutation is associated with a progressively higher age, in our study patients with the mutation had a higher median age than those without the mutation (47 vs. 39 years), but without statistical significance. Thus, the FLT3 mutation was detected in 27.5% of patients >55 years of age, similar to that reported by Derek et al. (36) where PCR detected FLT3 ITDs in 29% of the population >60 years of age. In this study the mutation was not associated with significant differences in OS, a finding similar to ours where the presence of the mutation in patients >55 years of age did not affect OS. A dismal prognosis per se is observed in patients with AML and advanced age mostly due to pre-existing co-morbidities (37).

On the other hand, there are few pediatric studies reporting FLT3 mutations. A study from Costa Rica (20) among 14 AML pediatric patients found a FLT3 mutated prevalence of 14.3%. In a pediatric Argentinean population, Alonso et al. (20) studied 92 AML patients and found the FLT3 mutation in 15.2%. Of these, 9.8% had ITD. In our study, children with FLT3 mutations represented only 7.1% and all had ITD/FLT3.

One additional controversial issue is the impact of FLT3 status in the M3 leukemia group because this entity has a better prognosis compared to the other AML. In a Brazilian series, among 31 patients with AML M3, the ITD/FLT3 frequency was 32%. In our study of 18 patients with AML M3, four had FLT3 mutations (22.2%) and two of these four died with a median survival of 1.8 months. One AML M3 patient is alive after 10 months since the time of diagnosis and currently is in complete remission. However, the true prognostic value of the mutation is attenuated in AML M3 by the benefit of treatment with all-trans retinoic acid (ATRA) and arsenic trioxide (ATO). Schnittger et al. (38) sought the prognostic impact of ITD/FLT3 mutations in patients with AML M3, finding the ITD/FLT3 mutation in 47/147 patients (32%) and the tyrosine kinase mutations (FLT3-TKD) in 19/147 patients (12.9%). These mutations had a prognostic impact only when allelic determination was made (ratio mutated/wild type <0.5) being associated with a better 2-year overall survival (86.7 vs. 72.7%, $p = 0.075$) and a greater event free survival rate (84.5 vs 62.1%, $p = 0.023$). In our M3 AML population with the FLT3 mutation, mortality was not influenced ($p = 0.28$).

Several working groups have tried to elaborate a ''prognostic model'' assessment using molecular and cytogenetic alterations with different results (10,39). Nevertheless, FLT3 as an independent prognostic indicator has been associated with an adverse outcome whenever this population has been subjected to HSCT (40). Our FLT3-mutated population treated with a HSCT had lower median survival probability compared with the

non-mutated population (5 vs. 36 months, $p = 0.0001$) supporting previous reports. In most Latin American populations, access to new targeted therapies is limited by financial issues; thus, chemotherapy and HSCT remain the only approaches for treating AML patients.

The length of the FLT3 mutations in general was <100 bp. Previous studies have described that longer mutations are associated with a worse prognosis. In our study a poor outcome was observed in the overall FLT3 mutated population in spite of the length of the mutation. In addition, we found a not previously reported nucleotide exchange of timine by cytosine at 66608 position of the FLT3 gene that causes valine to be replaced by histidine at the 615 position at the juxtamembrane domain of the FLT3 receptor.

It is important to mention that collaborative studies in Latin America are scarce and this could explain why there are few epidemiological data about AML and other hematological diseases in this region. This bi-national study is the first multicenter Latin American analysis describing molecular findings in AML. It is clear, therefore, that FLT3 status could be a simple and affordable tool to predict poor prognosis in developing countries limited by scarce health resources and could serve as indicator for early referral to stem cell transplantation centers. On the other hand, interesting findings in the CBC at diagnosis of AML patients having the FLT3 mutation include a greater WBC count, lower platelet count and higher hemoglobin level in comparison to patients who lack the mutation. Although these data are consistent with a trend to lower survival they did not reach statistical significance. Our data showed that a younger group age (<55 years) was associated with a worse outcome in our mutated population and the FLT3 mutated group had a lower OS than the non-mutated group.

In conclusion, FLT3-ITD mutation prevalence in AML patients was 20.3%, consistent with published data from Latin American and other populations. To complete the configuration of the AML molecular landscape in the region, larger multicenter studies on FLT3 and other important molecular markers in AML patients are needed.

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