# Characterization of Acute Lymphoblastic Leukemia in the Pediatric Mexican Mestizo Population

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## Abstract

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer. It is considered a widely heterogeneous disease caused by multiple somatic structural DNA rearrangements. In this report we tested the presence of fusion genes, TCF3-PBX1, KMT2A-AFF1, BCR-ABL1, and ETV6-RUNX1 in a pediatric Mexican mestizo population stratified by age and stage of cellular differentiation. The results showed the absence of these fusion genes in most of the cases, leading to the conclusion of the necessity to develop and validate new biomarkers.

## Background

Acute lymphoblastic leukemia (ALL) is the most common neoplasm of lymphoid progenitor cells in pediatric populations. ALL cases can be broadly classified as B-cell or T-cell. B-cell ALL (B-ALL) has many genetic subtypes characterized by major chromosomal alterations. Flow cytometry and biomarkers identification provide information about the subtype of ALL and can be correlated with the patient's prognosis. Based on reactivity with antigens present on the cellular surface or in the cytoplasm of leukemia cells, B-ALL can be divided into 4 subtypes according to its stage of differentiation: pro-B, common B, pre-B, and immature B subtypes. All of them comprise multiple entities defined by structural chromosomal rearrangements that results in chimeric fusion genes.

## Objective

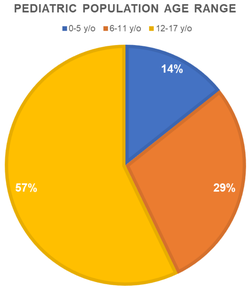
This study aims to establish the association of the molecular fusion genes TCF3-PBX1 t(1;19), KMT2A-AFF1 t(4;11), BCR-ABL1 t(9:22) and ETV6-RUNX1 t(12;21) with ALL subtypes according to its stage of differentiation.

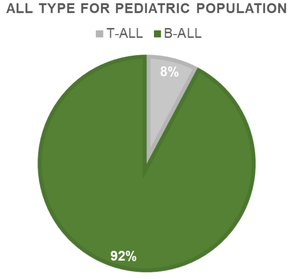
## Material & Methods

The study includes a retrospective analysis of laboratory data results from a pediatric population diagnosed with ALL during a 3-year period (2018–2021), referred to Mendel laboratories from different health institutions. Ninety ALL cases, age range 0–17 years, were classified by immunophenotype using fluorescent conjugated monoclonal antibodies and analyzed by flow cytometry (Beckman Coulter Cytometer). The presence of fusion genes (TCF3-PBX1, KMT2A-AFF1, BCR-ABL1, and ETV6-RUNX1) were tested by RT-PCR using total RNA isolated by standard protocols.

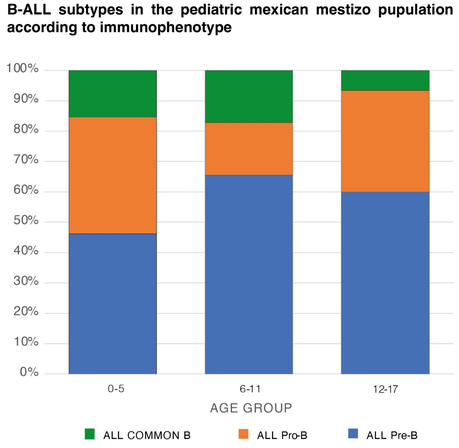
## Results

Total study population was divided into three age range groups, the peak age group for ALL was 12-17 years, which accounts for 57% of the cases. B-cell ALL represented 92% of the cases (83) and only 7 cases were classified as T-cell precursor lineage (T-ALL).

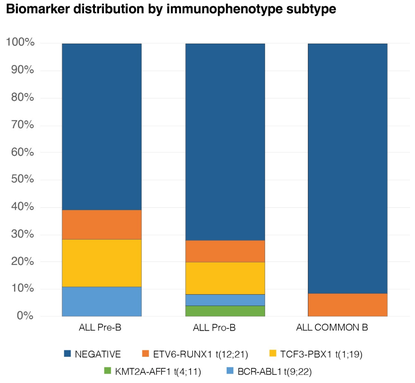



The B-cell ALL cases were dividen into three subtypes on the basis of antigen expression identified by flow cytometry. All three subtypes were present despite the group range being pre-B the most common.




The presence of fusion genes (TCF3-PBX1, KMT2A-AFF1, BCR-ABL1, and ETV6-RUNX1) were assayed in all samples. All biomarkers were identify in subtype pro-B cases. On the other hand, ETV6-RUNX1 was consistent as a unique biomarker in common B-ALL. Seventy-one percent of the cases did not showed the presence of any of the four biomarkers tested and correspond to quadruple negative cases. The low frequency of structural DNA rearrangements as fusion genes found in our study corroborate the high genetic variation of the disease.




## Discussion

The biomarkers TCF3-PBX1, rearrangement of MLL, BCR-ABL1, and ETV6-RUNX1 are decisive in establishing the prognosis of patients with any of the ALL-B subtypes and enable the definition of a stratified treatment. The absence of these markers prevails in our study population, so it is essential to determine the prognostic value of other recently described mutations (CRLF2, IKZF1 and JAK2) to improve personalized diagnosis and therapy.

## References

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