(OR = 3.03, 95% CI 1.76–5.21, p = 0.018). Dentre os 32 pacientes com fenótipos MI e ML, 19 iniciaram a fase de manutenção com a dose padrão de tiopurina. Por outro lado, dos 56 pacientes que iniciaram o tratamento com dose reduzida, apenas 13 eram MI ou ML. Contudo, 18 pacientes com fenótipo MI iniciaram o tratamento com dose usual e apresentaram diversos sintomas de toxicidade. Os ajustes de dose realizados ao longo do tratamento ocorreram somente pacientes com fenótipo MN. **Discussão e conclusão:** Os resultados sugerem que a adesão clínica ao resultado da genotipagem poderá ser importante para evitar manifestações de toxicidade ao longo do tratamento com tiopurinas. A associação significativa entre o SNP de ITPA e a NF é um dado inédito e ressalta a importância de considerar o potencial uso desse marcador na individualização do tratamento de nossas crianças. Este estudo reforça a relevância da farmacogenética na individualização da terapia em LLA pediátrica.

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ID – 2729

EVALUATION OF PRDM16 GENE EXPRESSION PROFILE IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute Lymphoblastic Leukemia (ALL) is the most common pediatric cancer worldwide, characterized by dysregulation in the proliferation and differentiation of the hematopoietic lineage. Early diagnosis is essential and includes the analysis of genetic biomarkers. Beyond existing molecular classifications, new research is focusing on epigenetic regulators such as the PRDM16 gene, whose alterations in leukemogenesis have been highlighted previously. **Objectives:** This study aimed to identify the *PRDM16* expression profile in pediatric ALL within an Amazonian cohort, associating it with clinical, laboratory, and molecular data. **Methods:** Eighty newly diagnosed pediatric patients treated at a reference hospital in Belém-Pará, were evaluated, considering clinical data (ALL subtype, biological sex, and age), laboratory parameters (leukocytes, hemoglobin, and platelets), and molecular biomarkers (*BCR::ABL1*, *TCF3::PBX1*, *KMT2A::AFF1*, *ETV6::RUNX1*, and *STIL::TAL1* gene fusions) (CAAE: 30307820.7.0000.5634). A control group of 8 healthy individuals was also included. Gene expression analysis was performed using the TaqMan® system, while gene fusion detection was assessed by Nested PCR. Statistical analyses were conducted using the Endogene Analyzer, PSPP v1.2, and Jamovi v2.3 platforms. **Results:** Among the studied cases, 71 exhibited detectable *PRDM16* expression levels, demonstrating its overexpression compared to controls (p = 0.001; FC = 10.21). *PRDM16* was found to be more dysregulated in the T-cell subtype (T-ALL) (p < 0.001; FC = 36.01) than in the B-cell subtype (B-ALL) (p = 0.024; FC = 6.46), with this trend supported by correlation analyses (p < 0.001; Spearman's ρ=0.514) and categorical association tests (p = 0.002; OR = 26.2; 95% CI 1.46–470). Additionally, lower *PRDM16* expression levels were associated with thrombocytosis (p = 0.025), showing a negative correlation (p = 0.027; Spearman's ρ = -0.461). Interestingly, a small subset of patients exhibited gene silencing (n = 9), which was associated with the absence of gene fusions (p = 0.033; OR = 0.12; 95% CI 0.01–1.02), with only one fusion case (*ETV6::RUNX1*) observed in this group. ROC curve analysis indicated that *PRDM16* effectively discriminates between B-ALL and T-ALL (AUC=0.95; 95% CI 0.90–0.99). **Discussion and conclusion:** PRDM16 overexpression is associated with ALL, particularly the T-cell subtype where its discriminatory power is high. The gene also showed a negative correlation with thrombocytosis. PRDM16 is an epigenetic transcriptional factor with histone methyltransferase and zinc fingers domains, whose imbalanced isoforms (PRDM16F/S) are linked to leukemogenesis. It participates in the pro-leukemic microenvironment and interacts with megakaryocytic pathways even in lymphoid leukemias. Cases of PRDM16 silencing in pediatric ALL have been previously associated with the absence of gene fusions, as confirmed in this study. Given the scarcity of molecular markers for pediatric T-ALL, PRDM16 emerges as a strong candidate for improved disease stratification. The identified associations highlight the complexity of PRDM16 regulation in pediatric ALL and the importance of considering both upregulation and silencing. This contributes to a deeper understanding of leukemic biology and advances future research and innovation in targeted therapies. **Financial support:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Pró-Reitoria de Pesquisa e Pós- Graduação (PROPESP/UFPA).

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ID – 2400

EXPRESSION PROFILE AND CLINICAL SIGNIFICANCE OF KIAA0125 IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute Lymphoblastic Leukemia (ALL) is the most common neoplasm in children worldwide, affecting approximately 54,000 people aged 0–19 years. This illness results in multiple complications, both disease and treatment related. On that note, patients frequently experience treatment resistance and relapses, as well as multiple side effects associated with available therapy regimens, which severely decrease their quality of life. To address this problem, there is urgent need for further research into enabling earlier diagnosis and refining therapeutic targeting. From that perspective, long non-coding RNAs (lncRNA) have shown their relevance in cancer biology research, for their major regulatory functions. Among them, KIAA0125 is a promising subject of study and has been proposed as a possible biomarker in ALL, delivering valuable insight for prognosis prediction. **Objectives:** Given the urge to improve the scenario of ALL, the aim of this study is to evaluate the role of KIAA0125 as a possible prognosis predictor or therapy target. **Methods:** To achieve that goal 79 Peripheral Blood (PB) or bone marrow samples from ALL patients and 8 PB samples from healthy volunteers (CAAE 30307820.7.0000.5634) were used. Groups consisted of individuals aged 0 to 17 years, of both sexes. RNA was extracted from the samples using TRIzol Reagent® and converted into cDNA using High-Capacity cDNA Reverse Transcription® kit. Gene expression was evaluated via RT-qPCR, using the Taqman® probe system for KIAA0125 and reference genes ACTB (Hs01060665_g1) and ABL1 (Hs01060665_g1). Then, the mean Cycle threshold (Ct), ΔCt, and Fold Change (FC) were calculated. Normality was assessed using the Shapiro-Wilk and D'Agostino Pearson tests; and Student's t or Welch tests were used to evaluate the differences in global expression levels between patients and healthy controls. Additionally, patients were stratified according to gene expression levels, based on fold change values: <0.15 was classified as very low expression, and > 0.15 as low or normal expression. Later, those categories were analyzed in relation to the patients' biochemical and hematological parameters. Statistical significance was set at $p \leq 0.05$, and analyses were conducted using PSPP v2.0.0 and Endogene Analyzer software. **Results:** The mean ΔCt in the control group was 3.94±1.23 cycles, lower than in the ALL group (6.83±3.10). Receiver Operating Characteristic (ROC) curve analysis indicated that KIAA0125 expression is a satisfactory marker for distinguishing ALL patients from healthy subjects (AUC=0.80). When evaluating fold change between groups, KIAA0125 expression was found to be significantly associated with patients' platelet counts (p=0.046), with median values much lower in patients with very low expression (70,500) than in those with low or normal expression (189,500). Spearman's correlation revealed a weak positive correlation between gene expression level and platelet count (rho=0.251). **Discussion and conclusion:** The observed association between low expression and reduced platelet counts, along with the weak positive correlation between expression levels and platelet count, suggests a possible link between KIAA0125 expression and disease severity. These findings support the potential utility of KIAA0125 as a biomarker for diagnosis and prognosis in pediatric ALL. **Financial support:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior e Pró-Reitoria de Pesquisa e Pós-Graduação/UFPA.

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FLOW CYTOMETRY IMMUNOPHENOTYPING FOR JUVENILE MYELOMONOCYTIC LEUKEMIA: EVALUATION OF 52 PATIENTS FROM BRAZILIAN COOPERATIVE GROUP OF PEDIATRIC MYELODYSPLASTIC SYNDROME

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Introduction: Juvenile Myelomonocytic Leukemia (JMML) is a rare myeloproliferative disease of childhood, recognized as an entity involving genes from the RAS-MAPK pathway. In JMML, Immunophenotyping (FCI) has been used for blast counting and evaluation of monocyte subtypes. It is controversy if this distribution is similar to that seen in Chronic Myelomonocytic Leukemia (CMML). Recently, we have reported a study on immunophenotyping in JMML at diagnosis. **Objectives:** To expand the immunophenotypic analysis, studying erythroid and monocytic maturation. **Methods:** 8-color antibody combinations were used, including CD64, IREM2, CD105, CD36 and CD71 in the previous panel. FCI findings were correlated with patients' molecular profile. **Results:** 52 JMML patients were evaluated: median age 17-months. PTPN11 (13) and KRAS (11) mutations were more frequent. Patients with CBL mutation, together with NRAS and KRAS subgroups were younger (p=0.026). Decrease of hematogones type I (median 0.6%) and T lymphocytes (median 3.4%), increase CD34+CD117+ (3.4%) and monocytes (12.2%) were similar between molecular subgroups. Abnormal expression of CD7 in myeloid progenitors was more frequent in PTPN11 patients. Erythroid and monocytic precursors were assessed in 24 patients. Monoblasts had a median of 14.9% and promonocyte were 29.5%, with higher percentages in NF1 and PTPN11 subgroups. Patients with NRAS, NF1 and absence of RAS mutations showed a low percentage of CD16+ monocytes and a higher percentage of CD14+CD16- monocytes (classical), similar to CMML, while PTPN11, KRAS and CBL patients had lower percentages of classical monocytes as found in MDS (p=0.02). **Discussion and conclusion:** We confirmed our previous results. CBL subgroup had similar features as other molecular profiles. JMML patients presented an increase of myeloblasts and early monocytic precursors, compatible with a more aggressive disease, intermediary between a chronic myeloid neoplasm and a progression to acute leukemia, more evident in PTPN11 and NF1 mutated patients. Despite examined in bone marrow, monocytes subsets analysis dont seem to be a diagnostic strategy for JMML. The features of FCI data should also be compared with the methylation profile.

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