

Research Article

Assessment of Redox Patterns at the Transcriptional and Systemic Levels in Newly Diagnosed Acute Leukemia

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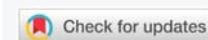
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Keywords: Acute leukemia; Gene expression; Redox biomarkers; Oxidative status; Inflammatory status



Abstract

Background: Acute leukemia is the result of clonal transformation and proliferation of a hematopoietic progenitor giving rise to poorly differentiated neoplastic cells. Reactive oxygen species play a role in maintaining the quiescence, self-renewal, and long-term survival of hematopoietic stem cells, but it is unclear how they would affect disease onset and progression. The aim is to evaluate, at the transcriptional and systemic level, the oxidative-inflammatory status in newly diagnosis acute leukemia patients.

Methods: Seventy acute leukemia patients [26 acute lymphoblastic leukemia (ALL), 13 Acute Promyelocytic Leukemia (APL), and 31 Acute Myeloid Leukemia (AML)] and forty-one healthy controls were analyzed. Malondialdehyde and catalase activity were evaluated. Gene expression of NRF2, SOD, PRDX2, CAT, IL-6, and TNF- α was analyzed by real-time PCR.

Results: Malondialdehyde concentration was similar in all groups studied. Catalase activity was significantly higher in AML and APL patients compared to controls, while ALL showed similar activity to the healthy group. NRF2, CAT, and PRDX2 expression levels were similar between groups, SOD expression was downregulated in all acute leukemia patients. TNF- α expression was lower in AML groups than in healthy individuals, and IL-6 mRNA expression was downregulated in ALL and APL.

Conclusion: This is the first report that correlates transcriptional and systemic parameters associated with the oxidative inflammatory status in newly diagnosed acute leukemia. Some of the parameters evaluated could be used as biomarkers in the selection of an effective therapeutic strategy and will open new directions for the follow-up and evolution of this disease.

Introduction

Acute Leukemia (AL) is the result of clonal transformation and proliferation of a hematopoietic progenitor that gives rise to poorly differentiated neoplastic cells [1]. The origin of AL is multifactorial and has not yet been entirely elucidated. This hematological malignancy begins in a bone marrow hematopoietic progenitor exposed to a complex interplay of hereditary and environmental factors which produces disturbances in progenitor cell growth, differentiation, and proliferation leading to the clonal expansion of bone marrow blasts and their infiltration into the peripheral blood [1].

Leukemias are classified based on onset (acute or chronic), the affected blood cell type (lymphoblastic/lymphocytic or myeloid/myelogenous), the maturity stage of the blood cell, and phenotypic expression of the disease [2]. Traditionally, diagnosis and classification have been based on specific morphological characteristics and stages of differentiation. More recently, the World Health Organization (WHO) provided an updated classification based on a combination of clinical symptoms, cell morphology, immunophenotype, and genetic abnormalities. However, a classification based on molecular pathogenesis is likely to be more informative,

provide better prognostic stratification, and guide targeted treatment [3].

Reactive Oxygen Species (ROS), such as hydrogen peroxide (H_2O_2) and superoxide anion radicals are produced by the redox microenvironment and cellular metabolic processes. These play a double role in biological systems, where they may be either advantageous or disadvantaged for living systems [4]. Diverse studies highlight the important role that ROS plays in maintaining Haemopoietic Stem Cell (HSC) quiescence, self-renewal, and long-term survival. In addition, the ROS role in the differentiation from haematopoietic stem cells to terminally differentiated myeloid progenitors was outlined. However, excessive ROS production can lead to an oxidative imbalance that is quite clear in several hematopoietic malignancies, including acute and chronic leukemias. Nonetheless, it is unclear how ROS would affect disease onset and progression [5]. Thus, the sensitivity of HSCs to the damage caused by oxidative stress plus the accuracy in which ROS levels must be regulated in hematopoietic stem cells and early progenitors supports the importance of the redox homeostasis signaling in hematopoiesis [6,7].

ROS have also been shown to regulate the accumulation of transcription factors in the nucleus, such as the nuclear factor erythroid 2-related factor 2 (NRF2) [8,9]. Interestingly, NRF2 participates in cellular response to oxidative stress, since they have the ability to bind Antioxidant Response Elements (ARE) and activate the expression of antioxidant and detoxifying enzymes [7]. Activation of these transcription factors can lead to the expression of over 500 different genes, including those for growth factors, inflammatory cytokines, chemokines, cell cycle regulatory molecules, and anti-inflammatory molecules. Thus, the aberrant expression of inflammatory cytokines [tumor necrosis factor (TNF- α), interleukin-1 (IL-1), IL-6] has also been reported to play a role in oxidative stress-induced inflammation. This sustained inflammatory/oxidative environment leads to a vicious circle, which can damage healthy neighboring epithelial and stromal cells and, over a long period of time, may lead to carcinogenesis [10].

Several clinical studies reported that Superoxide Dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) is the most important endogenous antioxidant-scavenging in the cell. The cell enzymatic protection acts by preventing the excessive formation of ROS and, consequently, avoiding the oxidative damage of proteins, lipids, and nucleic acids. Antioxidants can either be upregulated or downregulated in leukemia cells depending on specific scenarios. Hence, antioxidant defense in the cell proved to be of crucial importance in carcinogenesis and in the recurrence of cancer [11,12]. All these redox alterations could influence the properties and behavior of neoplastic cells, constituting the molecular basis underlying this hematological disorder. Thus,

despite the advances in the knowledge of physiopathology of haematological malignancies, the interplay between the oxidant-inflammatory status at the diagnosis and the response of cytoprotective mechanisms is still unknown. The aim of this work is to evaluate, at a transcriptional and systemic level, the oxidative inflammatory status in newly diagnosed AL patients.

Materials and methods

This study was carried out at the Instituto de Bioquímica Aplicada, Universidad Nacional de Tucumán (UNT) from August 2016 to November 2020. This study was approved by the Bioethics Committee of the Facultad de Medicina-UNT N° 82574/2016, Tucumán, Argentina and it was conducted in accordance with the Helsinki Declaration.

Subjects

Seventy AL patients (47 males and 23 females), aged 18 - 78, were recruited at diagnosis. AL patients were classified into three groups: 26 acute lymphoblastic leukemia (ALL), 13 Acute Promyelocytic Leukemia (APL), and 31 acute myeloid leukemia (AML). All AL was diagnosed by morphologic analyses, myeloperoxidase cytochemical, immunophenotype, and cytogenetic studies by the Provincial Health System of Tucumán. Variables such as infection, tumor lysis syndrome, and patient comorbidity at debut were considered, and notably, none of these conditions were detected in the participants included in our study.

Healthy controls ($n = 41$), 22 males and 19 females, were recruited at the Instituto de Bioquímica Aplicada - UNT.

The inclusion criteria were women and men aged ≥ 18 years with acute leukemia diagnosis who had not started antineoplastic treatment until the sample was collected. Healthy subjects had to be ≥ 18 years of age, had a normal blood count, had not received any medication, and had no history of any chronic disease. Quantitative determinations of blood cells were performed using a hematology analyzer Sysmex KX-21N (Kobe, Japan).

Written informed consent was obtained from all study participants, which complies with all privacy and data protection laws.

Sample collection

Blood specimens were collected into K2-EDTA-containing tubes and in BD Vacutainer® serum tubes with separating gel. After centrifugation (5000 rpm for 10 minutes), serum samples were immediately aliquoted and stored at $-20\text{ }^{\circ}\text{C}$ until analysis.

Gene expression

The RNA was isolated from whole blood anticoagulated with K_2 -EDTA using TRI Reagent® (Molecular Research Center,

Inc. Ohio) according to the manufacturer's instructions. The mRNA NRF2, SOD, peroxiredoxin-2 (PRDX2), CAT, IL-6, and TNF- α expression were analyzed by real-time reverse transcription-PCR (RT-qPCR) using a LightCycler z480 (Roche Diagnostics). RT-qPCR was performed in two steps using the ImProm-II™ Reverse Transcriptase System (Promega) for the cDNA synthesis and LightCycler® FastStart DNA Master SYBR Green I (Roche Diagnostics) for the qPCR reactions. Cycling conditions: 40 cycles of 95 °C for 15s, 56 °C - 60 °C for 15s (according to the gene), and 72 °C for 30s. At the end of the reaction, a melting curve was produced by slowly heating the sample from 60 to 95 °C.

The primers were taken from Franco, et al. [13] (CAT, PRDX2, and GAPDH), Zhao, et al. [14] (NRF2), Das, et al. [15] (SOD), and Han, et al. [16] (IL-6 and TNF- α). The primer sequences are summarized in Table 1.

The data obtained from the RT-qPCR were compared to the mRNA expression of the glyceraldehyde 3-phosphate dehydrogenase (GAPDH) gene as an endogenous control (relative quantification). The relative quantification of gene expression was calculated using the $2^{-\Delta Ct}$ method, that is: $[2^{-(Ct \text{ gene under study} - Ct \text{ GAPDH})}]$ [17].

Determination of lipid peroxidation

Lipid peroxidation in serum was determined by estimating malondialdehyde (MDA) as thiobarbituric acid reactive substances through the modified method of that described by Buege and Aust [18]. During peroxidation, the peroxides are decomposed to MDA, which can be detected by thiobarbituric acid in a colorimetric reaction. MDA was measured spectrophotometrically at 535 nm under acidic conditions solution (15% trichloroacetic acid, 0.375% TBA, 0.25 N HCL) and subsequent alkaline hydrolysis (3 N NaOH) in serum samples. The results were expressed as $\mu\text{mol/mL}$.

Catalase activity

The CAT activity was measured in serum by the Goth method [19] Spectrophotometric assay involved the decomposition of hydrogen peroxide by CAT enzyme in phosphate buffer (60 mmol/L; pH 7.4) with 65 $\mu\text{mol/mL}$ of hydrogen peroxide for 1 minute. The remaining H_2O_2 reacted

with the ammonium molybdate forming a yellow complex. Measurements were performed at 405 nm. CAT activity was expressed as nmols of H_2O_2 consumed/min/mg of protein.

Protein determination

Serum protein was measured by the colorimetric method of Biuret using Proti 2 commercial reagent (Wiener lab.) according to the manufactured recommendation. Measurements were performed at 540 nm. Results were expressed as mg/mL

Statistical analysis

Statistical analyses were performed using InfoStat V.2020 statistical software. The normal distribution data are reported as mean \pm SD and the non-normal data as median and quartiles (Q1 - Q3). The comparative study was performed using the non-parametric Kruskal-Wallis test. The association degree between the parameters in the different subgroups was also determined by the Spearman correlation. A significance level of $p < 0.05$ was adopted.

Results

Characteristics of patients

We evaluated 70 patients with AL diagnosis classified into three groups: ALL (21 men and 5 women); AML (21 men and 10 women) and APL (8 women and 5 men). The age, sex, and principal hematological characteristics of patients are summarized in Table 2. All groups showed a similar average age. In AL patients we observed a similar white blood cell count and blasts count in peripheral blood. In addition, in these groups anemia and thrombocytopenia were detected.

Redox systemic biomarkers

Malondialdehyde (MDA) is one of the most important cell damage biomarkers and it indicates lipid peroxidation. Serum MDA concentrations were similar in all groups evaluated. Thus, in different AL groups and healthy controls similar levels of lipoperoxidation were observed (Figure 1A).

CAT is involved in the reduction of H_2O_2 generated as a consequence of cellular metabolism, behaving as a cytoprotective. In our study, CAT enzyme activity was

Table 1: The primer sequences used for the RT-qPCR.

| Genes studied | Forward Primer Sequence (5' → 3') | Reverse Primer Sequence (5' → 3') |
|---------------|-----------------------------------|-----------------------------------|
| NRF2 | GAGAGCCAGTCTTCATTGC | TGCTCAATGTCCTGTTGCAT |
| PRDX2 | ACAAAGGGAAGTACGTGGTCCTC | GCTGAACGCGATGATCTCG |
| SOD | CACATCAACGCGCAGATCAT | CAGTGCAGGCTGAAGAGCTATCT |
| CAT | CCAAATACTCCAAGGCAAAGGT | CTCCAGCAACAGTGGAGAACC |
| IL-6 | GGTACATCCTCGACGGCATCT | GTGCCTCTTTGCTGCTTTTAC |
| TNF- α | CCGAGGCAGTCAGATCATCTT | AGTGCCTCCTCAGCTTGA |
| GAPDH | CCACATCGCTCAGACCCAT | AGTTAAAAGCAGCCCTGGTGA |

NRF2: Nuclear factor erythroid 2-related factor; PRDX2: Peroxiredoxin 2; SOD: Superoxide Dismutase; CAT: Catalase; IL-6: Interleukin 6; TNF- α : tumor necrosis factor-alpha; GAPDH: Glyceraldehyde-3-phosphate dehydrogenase.

Table 2: Hematological characteristics of patients.

| Variables | | CONTROL | ALL | APL | AML |
|-------------------------------|---|---------------|-----------------|-----------------|----------------|
| Number of cases | M | 22 | 21 | 5 | 21 |
| | F | 19 | 5 | 8 | 10 |
| Age (years) | | 33 \pm 2 | 30 \pm 2 | 40 \pm 6 | 43 \pm 3 |
| WBC ($\times 10^9/L$) | | 6,8 \pm 0,3 | 42,6 \pm 12,0 | 30,4 \pm 11,4 | 36,5 \pm 8,2 |
| Hb (g/L) | M | 149 \pm 1 | 80 \pm 6* | 75 \pm 5* | 76 \pm 4* |
| | F | 132 \pm 1 | 79 \pm 6* | 80 \pm 10* | 72 \pm 7* |
| Platelets ($\times 10^9/L$) | | 228 \pm 7 | 67 \pm 14* | 29 \pm 6* | 34 \pm 6* |
| Blasts (%) | | | 54 \pm 6 | 67 \pm 8 | 46 \pm 5 |

ALL: Acute Lymphoblastic Leukemia; APL: Acute Promyelocytic Leukemia; AML: Acute Myeloid Leukemia; M: Male; F: Female; WBC: White Blood Cell Count; Hb: Hemoglobin. Data are presented as media \pm standard error. *Significant difference $p < 0,05$ with respect to the control group.

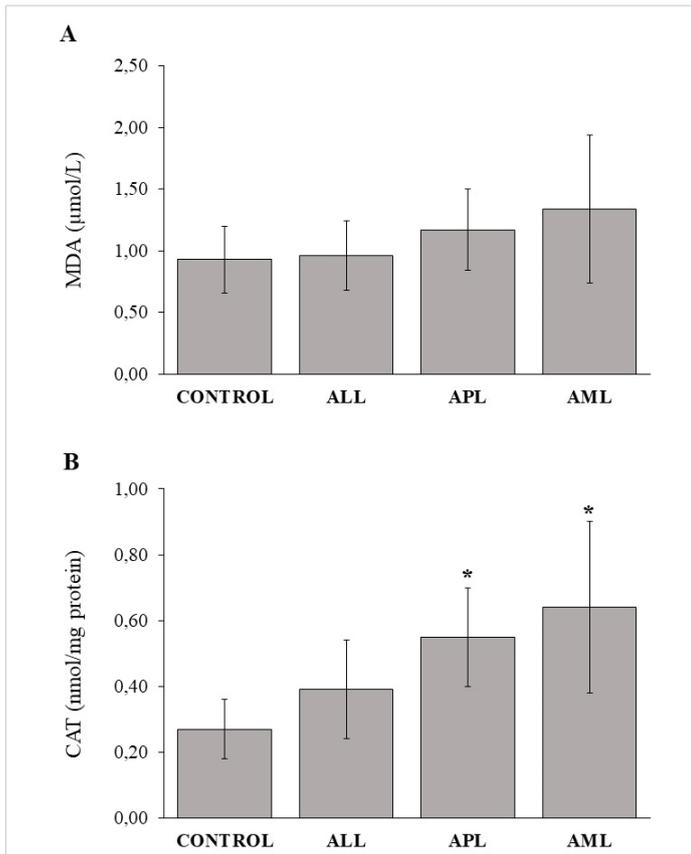


Figure 1: Redox parameters evaluation in serum. (A) Serum malondialdehyde (MDA) concentration. (B) Serum catalase (CAT) enzyme activity. ALL: Acute Lymphoblastic Leukemia; APL: Acute Promyelocytic Leukemia; AML: Acute Myeloid Leukemia. Each column represents the group media ± standard deviation. *Significant difference $p < 0,05$ with respect to the control group.

significantly higher in the AML and APL patients with respect to the healthy controls, while ALL showed similar CAT activity then the control (Figure 1B).

Redox gene expression

We evaluated the transcription factor NRF2 involved in cellular response to oxidative stress. Results showed no significant difference between NRF2 expression in AL groups and control (Table 3). In addition, we study mRNA expression of the PRDX2, CAT, and SOD enzymes. While CAT and PRDX2 expression levels were similar between groups, SOD expression was downregulated in all AL patients.

The current study shows that NRF2 presents a different degree of association with its target genes according to the subtype of pathology (Table 4). In the APL group, the highest degree of positive associations were found between NRF2 and antioxidant enzymes encoding target genes, NRF2 vs. PRDX2 ($r_s = 0,86^*$) and NRF2 vs. SOD ($r_s = 0,81^*$). The association NRF2 vs. CAT ($r_s = 0,41^*$) was moderately positive in the AML, while in the other leukemia, there were no observed significant differences.

Cytokine expression

The pro-inflammatory TNF- α and IL-6 mRNA expression

Table 3: Relative gene expression of NRF2 transcription factor and antioxidant enzymes in the different subtypes of acute leukemia.

| Genes studied | CONTROL | ALL | APL | AML |
|---------------|-----------------------|------------------------|---------------------------|------------------------|
| NRF2 | 0,23 (0,07 - 0,63) | 0,07 (0,03 - 0,40) | 0,06 (0,03 - 1,41) | 0,23 (0,07 - 0,40) |
| PRDX2 | 0,14 (0,07 - 0,99) | 0,16 (0,02 - 0,28) | 0,07 (0,02 - 0,33) | 0,17 (0,03 - 0,52) |
| SOD | 1,16 (0,39 - 3,61) | 0,07* (0,02 - 0,38) | 0,02* (3,4E-03 - 0,23) | 0,05* (0,01 - 0,34) |
| CAT | 0,30 (0,03 - 2,27) | 0,09 (0,01 - 0,29) | 0,30 (0,10 - 0,50) | 0,13 (0,02 - 0,50) |

ALL: Acute Lymphoblastic Leukemia; APL: Acute Promyelocytic Leukemia; AML: Acute Myeloid Leukemia; NRF2: Nuclear factor erythroid 2-related factor; PRDX2: Peroxiredoxin 2; SOD: Superoxide Dismutase; CAT: Catalase. Data are presented as median (Q1 - Q3). *Significant difference $p < 0,05$ with respect to the control group.

Table 4: Association between transcription factor NRF2 and its target genes in different subtypes of acute leukemia.

| Associations | ALL | | APL | | AML | |
|------------------------|-------|-----------|-----------------------|-----------|-------|-----------|
| | r_s | p - value | r_s | p - value | r_s | p - value |
| NRF2 vs. PRDX2 | 0,55* | 0,0063 | 0,86* | 0,0030 | 0,54* | 0,0028 |
| NRF2 vs. SOD | 0,46* | 0,0204 | 0,81* | 0,0048 | 0,30 | 0,1045 |
| NRF2 vs. CAT | 0,20 | 0,3157 | 0,48 | 0,0977 | 0,41* | 0,0261 |
| NRF2 vs. IL-6 | 0,27 | 0,1796 | -2,80E ⁻⁰³ | 0,9929 | 0,59* | 0,0012 |
| NRF2 vs. TNF- α | 0,52* | 0,0093 | 0,63* | 0,0286 | 0,09 | 0,6161 |

ALL: Acute Lymphoblastic Leukemia; APL: Acute Promyelocytic Leukemia; AML: Acute Myeloid Leukemia; NRF2: Nuclear factor erythroid 2-related factor; PRDX2: Peroxiredoxin 2; SOD: Superoxide Dismutase; CAT: Catalase; IL-6: Interleukin 6; TNF- α : Tumor Necrosis Factor-Alpha; r_s : Spearman's Correlation Coefficient. *Significant association $p < 0,05$.

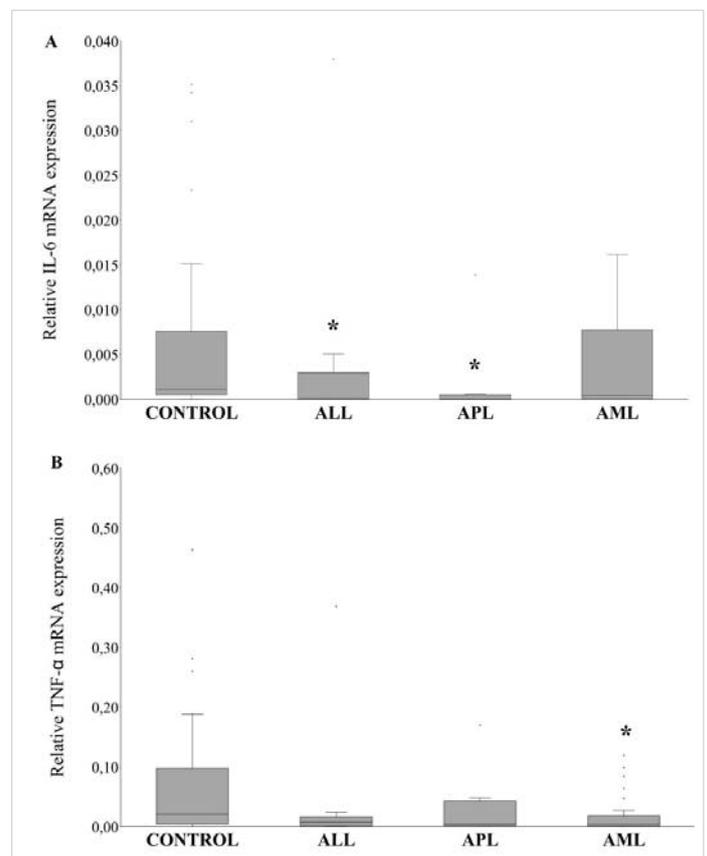


Figure 2: Transcriptional analysis of pro-inflammatory cytokines. (A) qRT-PCR expression of IL-6 on human peripheral blood leukocytes. (B) qRT-PCR expression of TNF- α on human peripheral blood leukocytes. ALL: Acute Lymphoblastic Leukemia; APL: Acute Promyelocytic Leukemia; AML: Acute Myeloid Leukemia. *Significant difference $p < 0,05$ with respect to the control group.

were investigated. In three AL groups, TNF- α expression was lower than in healthy individuals, however, only AML patients showed significant values being diminished compared to the control group (Figure 2). The IL-6 mRNA expression was downregulated in ALL and APL, while in AML showed similar levels than the control group.

The NRF2 influence in cytokines gene expression in different ALs was evaluated (Table 4). NRF2 vs. TNF- α association was moderately positive in ALL ($r_s = 0,52^*$) and APL ($r_s = 0,63^*$) while the NRF2 vs. IL-6 correlation was moderately positive only for the AML group ($r_s = 0,59^*$).

Discussion

Acute leukemia is characterized by great heterogeneity at the hematologic level, as well as an evolution and response to treatment variables. Despite the increasing use of different markers for their characterization, there are some aspects that have not yet been elucidated. Thus, AL is a hypercatabolic state with excess generation of free radicals leading to a redox imbalance. These alterations in oxidative stress metabolism could be associated with tumor cells and also impact negatively on the ongoing disease. In the present study, we analyzed some biomarkers associated with redox balance. Published reports showed a higher systemic level of MDA in AL, so we studied the lipid peroxidation status, determining this parameter in patients with AML, ALL, and APL. Our results show that MDA levels in the three groups of AL studied do not present significant differences compared to healthy individuals, however, the data tended to be higher in AML and APL, while in ALL the behavior was similar to the control group. In contrast, Rasool, et al. [5] showed elevated levels of MDA in ALL and AML compared with the control [5]. These differences could be due to the fact that our study includes the differential classification between AML and APL as well as a larger number of patients with AML. On the other hand, in this work, the higher CAT activity in AML and APL evidenced a redox imbalance [20]. This fact could be due to the requirement of the organism to increase the antioxidant defense mechanisms in this pathological state. Based on the results obtained, we decided to evaluate CAT expression as well as other antioxidant enzymes, SOD and PRDX2, in peripheral blood white cells. This evaluation showed that there is no variation of CAT mRNA expression with a higher systemic CAT activity at the leukemia debut which might reflect a pathological state and a dysregulated redox balance.

SOD mRNA expression, another important antioxidant, showed a marked decrease in leukemia patients. In this regard, previous work demonstrated that SOD activity was decreased in AL at the time of diagnosis [5,21,22]. In a study performed in patients with bladder cancer, the activity and expression of some antioxidant genes, such as CAT, SOD and glutathione peroxidase 1 (GPX 1), were evaluated. It was observed that the correlation between activity and expression

was variable according to the enzyme considered [23]. In our work, a similar result was observed with CAT activity and its expression. This fact shows an asynchronism between antioxidant gene expression and their systemic activity in a neoplastic state. In addition, PRDX2 tended to have low expression in the leukemia patient groups, especially in ALL and APL. Gosfrey, et al. (2012) reported that a low PRDX2 expression is clinically associated with poor prognosis in AML patients [24].

The relationship between oxidative stress and inflammation has been documented by many authors [25,26]. Inflammation is a natural defense mechanism associated with many disorders, including neoplastic processes such as those considered in this work. TNF- α and IL-6 have been described as key pro-inflammatory cytokines impacting the function of hematopoietic cells and promoting inflammatory diseases [27-29]. Thus, pro-inflammatory IL-6 and TNF- α cytokines mRNA expression was evaluated. IL-6 is a pleiotropic multifunctional cytokine that, besides its important function as an acute phase protein in inflammation [30], plays a key role within the network of cytokines involved in the regulation of hematopoiesis and leukemic blast formation [31-33]. Our findings showed decreased TNF- α and similar IL-6 expression in AML compared with healthy individuals. Another study revealed similar TNF- α expression with higher IL-6 mRNA expression compared with the control group [34]. These results could be due to the fact that in our study we discriminated AML into two separate groups: APL and AML. In addition, the results could also be affected by the number of patients who participated in the study and by the ethnicity to which they belong. In our case, the patients come with a diverse genetic background which might be significant when compared to that from the aforementioned study which was conducted in China, a culturally and genetically different population.

On the other hand, in ALL and APL the expression level of IL-6 was decreased. Allahbakhshian Farsani, et al. [35] (2020), reported that the mRNA level of this gene was significantly lower in T-ALL patients as compared to the control group, while in the ALL group (B-ALL plus T-ALL) had no significant differences with respect to healthy subjects. The number of healthy subjects in our study was higher than in the previous report and this fact would contribute to the difference in IL-6 levels of ALL patients. In addition, previous reports showed that low-level serum of IL-6 in ALL individuals represents favorable prognostic factors for the patients [36,37]. The downregulation of mRNA IL-6 detected in our study could be associated with a good prognosis in ALL and APL patients.

NRF2 has an essential role in activating enzymes in response to oxidative stress, such as PRDX2, CAT, SOD, and pro-inflammatory TNF and IL-6 cytokines [38]. Thus, we evaluated the associations between NRF2 with parameters before mentioned in different types of AL. Impaired

antioxidant defenses in acute leukemia would have adverse consequences on disease progression. The associations evaluated reflect an increase in antioxidant forces contributing to minimizing oxidative stress: NRF2 vs. PRDX2 in the three AL types; NRF2 vs. SOD in APL ($r = 0,81$) and ALL ($r = 0,46$); NRF2 vs. CAT in AML ($r = 0,41$). The positive correlation of NRF2 with antioxidant genes suggests the vital role of the NRF2 pathway, favoring redox balance. Leukemic cells live under oxidative stress and it is considered that an excessive level of ROS can contribute to cell proliferation and transformation. In our study, we observed the highest positive association between NRF2 and antioxidant enzymes (PRX2 and SOD) in APL. These findings would indicate that the antioxidant forces in APL could be favored at diagnosis compared to other types of AL studied. Modulation of ROS levels could be useful as a strategy to improve response to treatment, decrease cytotoxicity, and prevent early relapse. The activation of the NRF2/TNF pathway detected in ALL and APL and NRF2/IL-6 in AML would be due to the inflammatory response induced at the initial stage of leukemia. These gene activations showed different behavior according to the type of leukemia considered.

The systemic assessment of the parameters studied at the transcriptional level is important to highlight the knowledge of the relationships involved in oxidative stress and inflammation in newly diagnosed acute leukemia patients. Considering that mRNA expression and associated protein levels may or may not be correlated, further studies are needed to select the most clinically useful parameters for the prognosis of each type of leukemia.

Conclusion

Our finding represents one of the first reports that correlate transcriptional and systemic parameters associated with oxidative inflammatory status in acute leukemia at the debut moment. Some of the parameters evaluated could be used as biomarkers in the selection of an effective therapeutic strategy and will open new directions for the follow-up and evolution of this disease as well as the associated complications.

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Data availability

All data generated or analyzed during this study are included in this published article.

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