Kirkuk Journal of Medical Sciences

ORIGINAL ARTICLE

miR-5192 Downregulation in Pediatric Leukemia: A Subtype-Specific Analysis

Zahraa Talib Ahbail [1,*], Anfal Mohammed Khudhair [1], Maysaa Nihad Ibrahim [2]

[1]*Department of Microbiology, College of Medicine, University of AL-Iraqia, Baghdad, Iraq*
[2]*Department of Pediatrics, College of Medicine, University of AL-Iraqia, Baghdad, Iraq*

[*]*Corresponding author email: zahraa.t.aubail@aliraqia.edu.iq*

Received: 21 November 2025
Accepted: 14 February 2026
First published online: 21 February 2026

How to cite this article:
Ahbail ZT, Khudhair AM, Ibrahim MN. miR-5192 downregulation in pediatric leukemia: a subtype-specific analysis. *Kirkuk Journal of Medical Sciences*. 2026;14(1):16–24.
DOI: 10.32894/kjms.2026.167312.1241

ABSTRACT

Background: MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression. Depending on context, they may act as tumor suppressors or oncogenes and therefore represent potential biomarkers for early detection, classification, and prognosis of childhood leukemia. This study aimed to evaluate the expression of miR-5192 in pediatric leukemia.

Methods: This case–control study included 50 children with leukemia and 50 apparently healthy controls aged 1–13 years. miR-5192 expression was quantified using real-time polymerase chain reaction (RT-qPCR).

Results: miR-5192 expression was significantly lower in leukemic children than in controls (-1.91 ± 4.62414 vs. -0.10 ± 2.80491, respectively; $p = 0.020$). Differences in miR-5192 expression were also observed among leukemia subtypes.

Conclusion: miR-5192 is downregulated in pediatric leukemia, supporting a potential tumor-suppressor role. Downregulation appeared consistent in acute myeloid leukemia (AML) and T-acute lymphoblastic leukemia (T-ALL), whereas its association with B-acute lymphoblastic leukemia (B-ALL) remains uncertain.

Key words: Pediatric leukemia; MicroRNAs; miR-5192

ISSN: 2790-0207 (Print), 2790-0215 (Online).

INTRODUCTION

Pediatric leukemia is the most common malignancy in children younger than 15 years, accounting for approximately 33% of all childhood cancers and 31% of childhood cancer deaths. It is characterized by the uncontrolled proliferation of immature leukocytes in the bone marrow, leading to disruption of normal hematopoiesis and immune function. The four major types of leukemia are acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL). Among these, ALL is the most frequent in children, representing approximately 75–80% of pediatric leukemia cases [1].

In Iraq, ALL is more common in children, whereas AML is more prevalent in adults; However, both subtypes can occur at any age. Reported proportions vary by region and time period: ALL accounts for approximately 55% of acute leukemia cases and AML for about 36%, with higher rates often reported in Baghdad [2]. The precise etiology of leukemia remains unclear, but both environmental and genetic factors increase risk, including benzene exposure, Down syndrome, ionizing radiation, and prior chemotherapy [3].

MicroRNAs (miRNAs or miRs) are endogenous, small (19–22 nucleotides), single-stranded, non-coding RNAs that regulate gene expression at the post-transcriptional level and play a central role in epigenetic regulation. They participate in essential biological processes, including cell proliferation, differentiation, apoptosis, and maintenance of cellular homeostasis. Dysregulated miRNA expression is a well-established feature of both solid and hematologic malignancies, where miRNAs may function as oncogenes or tumor suppressors by targeting key regulatory genes [4, 5].

In cancer, tumor-suppressive miRNAs are frequently downregulated through promoter hypermethylation, genomic deletions, mutations, or defects in miRNA biogenesis, which can lead to aberrant activation of oncogenic pathways [6]. In leukemia, miRNAs regulate critical pathways involved in hematopoietic stem cell differentiation, lineage commitment, and leukemic transformation. Several miRNAs, including miR-15a/16-1, miR-34a, miR-155, and miR-181, have been implicated in controlling apoptosis, cell-cycle progression, and immune signaling in leukemic cells [7, 8]. Consequently, miRNAs have emerged as promising biomarkers for diagnosis, subclassification, and prognosis, as well as potential therapeutic targets, particularly in pediatric ALL, where precise regulation of hematopoietic differentiation is essential [9].

Among regulatory miRNAs, miR-5192 remains poorly characterized in pediatric leukemia, and available data on its expression patterns and functional relevance are limited. Nonetheless, its predicted regulatory roles suggest that miR-5192 may influence genes involved in key oncogenic processes, including proliferation, resistance to apoptosis, and differentiation arrest—hallmarks of leukemogenesis. Through dysregulation of hematopoietic gene networks, miR-5192 may exert biological effects similar to those of other leukemia-associated oncogenic or tumor-suppressive miRNAs. Accordingly, this study provides an initial characterization of miR-5192 expression in pediatric leukemia and establishes a foundation for further investigation into its potential biological significance [10].

From a pathogenic perspective, altered miR-5192 expression may affect transcription factors and signaling cascades essential for hematopoietic lineage commitment and leukemic blast survival, potentially influencing pathways related to cell-cycle regulation, apoptotic signaling, and differentiation control. These mechanisms parallel those described for other leukemia-associated miRNAs that modulate leukemic cell behavior and disease progression [11].

Therefore, the present study aims to characterize miR-5192 expression in pediatric leukemia and to provide preliminary insight into its potential biological role. By establishing baseline expression patterns, this work seeks to support future investigations into the relevance of miR-5192 as a diagnostic or prognostic marker in leukemogenesis.

Materials and Methods

- **Study design and participants**

  This case–control study included 100 children: 50 leukemia cases and 50 apparently healthy controls. Leukemia cases were recruited from pediatric patients diagnosed at the Central Teaching Hospital of Pediatrics, Baghdad, between November 2024 and February 2025. Controls were recruited from the general Baghdad population and had no reported history of leukemia, other hematological malignancies, or chronic systemic disease. Control health status was assessed by parental interview and medical history, confirming no known blood disorders, chronic illnesses, acute infection, inflammatory conditions, or recent hospitalization at the time of enrollment. Routine laboratory investigations, including complete blood count (CBC), were not performed for controls. Children with a reported history of acute infection, inflammatory disease, or recent hospitalization were excluded.

- **Matching and eligibility criteria**

  Age and sex matching was attempted to reduce confounding; however, complete matching was not feasible because of practical limitations in recruiting healthy pediatric controls. Participants were aged 1–13 years, and 45% were in the 7–10-year age group. A statistically significant difference in mean age (p = 0.018) and age-group distribution

(p = 0.049) was observed between cases and controls; this partial age imbalance was acknowledged as a study limitation.

With respect to sex distribution, cases showed a slight male predominance, whereas controls were slightly female predominant; however, the difference was not statistically significant ($p > 0.05$), indicating comparable sex distribution between groups.

Inclusion criteria comprised all children diagnosed with leukemia, regardless of age, sex, or leukemia subtype. Diagnosis was established by hematologists based on bone marrow examination. Blood samples were collected during or after chemotherapy (not necessarily at initial diagnosis), and participants were included irrespective of disease duration. Relapse status was not used as a selection criterion because of limited clinical data availability.

Children who declined participation or for whom sufficient clinical information or an adequate sample could not be obtained were excluded.

To minimize selection bias, cases and controls were recruited from the same geographic area and during the same period. All samples were processed using identical laboratory procedures to reduce measurement bias.

- **RNA extraction and cDNA synthesis**

miR-5192 expression was quantified by quantitative real-time PCR (RT-qPCR) using an Agilent Technologies Stratagene Mx3000P qPCR system (Agilent Technologies, Germany). Total RNA was extracted from whole blood using the TRIzol method (Trans Company, China). Briefly, samples were lysed in TRIzol reagent, followed by chloroform phase separation. The aqueous phase was collected, RNA was precipitated with isopropanol, washed with 75% ethanol, and resuspended in RNase-free water. RNA concentration and purity were assessed using a NanoDrop spectrophotometer.

For efficient reverse transcription of miRNA, extracted RNA was poly(A)-tailed using a commercial poly(A) tailing kit (Trans Company, China). Reverse transcription was performed using a complete real-time RT master mix (Agilent Technologies, Germany) to synthesize first-strand cDNA under standard thermal conditions. This poly(A)-tailing strategy enables reverse transcription using an oligo(dT)-containing universal adaptor primer, followed by qPCR amplification with an miRNA-specific forward primer and a universal reverse primer. cDNA was used immediately or stored at −20°C until analysis.

- **RT-qPCR amplification**

RT-qPCR was performed using Universal Super SYBR Green Master Mix (Fisher Scientific, USA) in a final reaction volume of 20 µL. Each reaction contained 10 µL of 2× SYBR Master Mix, 0.5 µL of forward primer (final concentration 0.25 µM), 0.5 µL of reverse primer (final concentration 0.25 µM), 5 µL of cDNA template (1–10 ng), and nuclease-free water to volume. Cycling conditions are shown in (Table 1).

Primers were designed using NCBI bioinformatics tools to ensure target specificity (Table 2). Specific amplification was confirmed by melt-curve analysis showing a single peak without primer-dimer formation. No-template controls were included in each run to exclude nonspecific amplification.

- **Normalization and relative expression analysis**

Gene expression was normalized to U6 small nuclear RNA (U6 snRNA) as the endogenous reference. Relative miRNA expression was analyzed using the comparative Ct ($\Delta\Delta Ct$) method [12]. ΔCt values were calculated as:

$$\Delta Ct = Ct(\text{miR-5192}) - Ct(\text{U6})$$

and

$$\Delta\Delta Ct = \Delta Ct_{\text{case}} - \overline{\Delta Ct}_{\text{controls}}.$$

For interpretation, fold change (case relative to controls) can be derived as $2^{-\Delta\Delta Ct}$; therefore, $\log_2$ fold change equals $-\Delta\Delta Ct$. Results are presented as $\log_2$ fold change ($-\Delta\Delta Ct$), where negative values indicate downregulation and positive values indicate upregulation relative to controls; 0 indicates no change.

Table 1. RT-qPCR cycling conditions.

Step	Temp. (°C)	Duration	Cycles
Initial denaturation	95	2 min	1
Denaturation	95	15 s	40
Annealing	60	30 s	40
Extension	72	30 s	40
Melt curve	65–95	Variable	1

Table 2. Primer sequences of miRNA genes.

Gene/miRNA	Primer	Nucleotide sequence (5′-3′)
miR-5192	Forward	TAGTTCCAGCCTCCTGGCTC
	Reverse	GTACCAAGCCCTCACCACC
U6 snRNA	Forward	AACGCTTCACGAATTTGCGT
	Reverse	CTCGCTTCGGCAGCACA

- **Statistical analysis**

Data were entered and analyzed using SPSS version 26 and Statistica version 12. Continuous variables were summarized as mean ± SD and categorical variables as number (percentage). Between-group comparisons were performed using the independent-samples Student's t-test for continuous variables and the chi-square test

or likelihood-ratio test for categorical variables, as appropriate. Independent two-sample *t*-tests were used to compare miR-5192 expression between each leukemia subtype and controls, and one-way ANOVA was used for inter-subtype comparisons ($p = 0.032$). A two-sided p value < 0.05 was considered statistically significant.

- **Age-adjusted analysis**
  Because cases and controls differed significantly by age, an age-adjusted analysis was performed using an ANCOVA/linear regression framework with $\Delta\Delta Ct$ as the continuous outcome and study group (leukemia vs. control) and age (years) as predictors. Adjusted group effects are reported as regression coefficients (β) with 95% confidence intervals. As a conservative sensitivity approach, p values based on heteroskedasticity-consistent robust standard errors (HC3) were also reported.

- **Age-adjusted subtype analysis**
  Subtype-specific age-adjusted models were fitted to evaluate whether miR-5192 dysregulation differed by leukemia subtype. Separate ANCOVA/linear regression models were run with $\Delta\Delta Ct$ as the outcome and subtype (subtype vs. control) plus age (years) as predictors for major subtypes (B-ALL, AML, and T-ALL). Results are presented as β coefficients with 95% confidence intervals and p values. Robust HC3 standard errors were used as a sensitivity analysis. Due to insufficient sample size, CML cases ($n = 1$) were excluded from inferential and age-adjusted analyses.

RESULTS

A total of 100 children were enrolled in this 1:1 case–control study, comprising 50 leukemia cases and 50 healthy controls, all selected according to predefined inclusion and exclusion criteria. Participants were 1–13 years old, with an overall mean age of 7.44 ± 3.33 years.

The mean age of cases was significantly lower than that of controls (6.65 ± 3.27 vs. 8.22 ± 3.23 years; $t = 2.410$, $p = 0.018$). Participants were categorized into mutually exclusive age groups (1–2, 3–6, 7–10, and 11–13 years). The age-group distribution differed between cases and controls (Likelihood Ratio = 3.882, $p = 0.049$), with a higher proportion of controls in the oldest group (11–13 years), reflecting practical challenges in recruiting healthy pediatric controls. Nevertheless, most participants in both groups were 7–10 years old (44% of cases and 46% of controls).

Regarding sex, the overall study population showed a slight male predominance (51% male vs. 49% female; male-to-female ratio = 1.04:1). Although males were more frequent among cases and females among controls, the difference was not statistically significant ($p > 0.05$), indicating comparable sex distribution between groups. Accordingly, sex was not included as a covariate in the age-adjusted analyses (Table 3).

With respect to leukemia subtype distribution, acute lymphoblastic leukemia (ALL) was the most common diagnosis (42/50; 84%), comprising precursor B-ALL (B-ALL; 30/50; 60%) and precursor T-ALL (T-ALL; 12/50; 24%). Acute myeloid leukemia (AML) accounted for 7 cases (14%), and chronic myeloid leukemia (CML) for 1 case (2%) (Figure 1). Due to the very small number of CML cases ($n = 1$), CML was excluded from age-adjusted statistical analyses. Leukemia subtypes were assigned by the attending hematologist according to the WHO 2022 classification. Owing to the limited number of AML cases, further subdivision into FAB M1/M2/M3 categories was not performed.

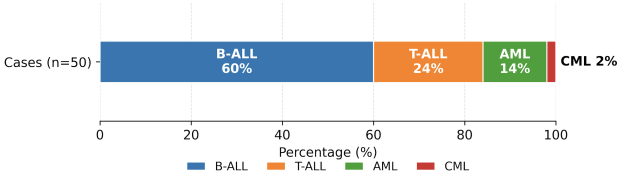

Figure 1. Distribution of leukemia types among study cases ($n = 50$), classified according to the WHO 2022 classification. *Source:* WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. 5th ed. Lyon, France: International Agency for Research on Cancer (IARC); 2022.

miRNA-5192 expression

miR-5192 expression was significantly lower in the case group than in controls (-1.91 ± 4.62414 vs. -0.10 ± 2.80491), with a mean difference of 1.80700 ($t = 2.363$, df= 98, $p = 0.020$) (Table 4). Gene expression was analyzed using the comparative Ct ($\Delta\Delta Ct$) method. For interpretation, fold change can be derived as $2^{-\Delta\Delta Ct}$ (and $\log_2$ fold change as $-\Delta\Delta Ct$). SD: standard deviation; a: unpaired t-test performed on $\Delta\Delta Ct$ values; df: degrees of freedom.

Age-adjusted comparison

Given the significant age difference between groups, an age-adjusted ANCOVA/linear regression analysis was performed. After controlling for age, leukemia status remained significantly associated with lower miR-5192 expression (Adjusted $\beta = -2.04$, 95% CI -3.60 to -0.47; $p = 0.011$). Using HC3 heteroskedasticity-consistent robust standard errors, the association remained statistically significant ($p_{robust} = 0.014$), indicating that age alone did not explain the observed downregulation.

The age-adjusted association between leukemia status (overall and by major subtype) and miR-5192 expression is summarized in (Table 5). Models included age (years)

Table 3. Baseline characteristics of the study sample.

Characteristic	Cases (n=50)	Controls (n=50)	Total (n=100)	Significance
Age (years)				
Mean ± SD	6.65 ± 3.27	8.22 ± 3.23	7.44 ± 3.33	t = 2.410, p = 0.018[a]
Range (min–max)	1–13	1–13	1–13	
Age group (years), n (%)				
1–2	4 (8%)	4 (8%)	8 (8%)	Likelihood ratio = 3.882,
3–6	18 (36%)	9 (18%)	27 (27%)	p = 0.049[b]
7–10	22 (44%)	23 (46%)	45 (45%)	
11–13	6 (12%)	14 (28%)	20 (20%)	
Sex, n (%)				
Female	21 (42%)	28 (56%)	49 (49%)	χ^2 = 1.961, df= 1,
Male	29 (58%)	22 (44%)	51 (51%)	p = 0.161[b]

Values are presented as mean ± SD or n (%).
[a] Unpaired t-test.
[b] Likelihood ratio (alternative chi-square) test.

Table 4. Mean comparison of miR-5192 expression ($\log_2$ fold change, $-\Delta\Delta Ct$) between study groups (n = 100).

Expression (Mean ± SD)	Leukemia cases (n=50)	Controls (n=50)	Mean difference (Controls−Cases)	Significance[a]
$\log_2$ fold change ($-\Delta\Delta Ct$)	−1.91 ± 4.62	−0.10 ± 2.80	1.81	t = 2.363, df= 98, p = 0.020

Expression values are presented as $\log_2$ fold change ($-\Delta\Delta Ct$) derived from the comparative Ct method [12]. Negative values indicate downregulation and positive values indicate upregulation relative to controls. SD: standard deviation; df: degrees of freedom.
[a] Unpaired t-test performed on $\log_2$ fold change ($-\Delta\Delta Ct$) values.

Table 5. Age-adjusted differential expression of miR-5192 ($\log_2$ fold change, $-\Delta\Delta Ct$) in pediatric leukemia overall and by major subtypes compared with healthy controls.

Comparison	n_{cases}	$n_{controls}$	Adjusted β	95% CI (low)	95% CI (high)	p-value	Robust p (HC3)
Leukemia (all) vs Control	50	50	-2.04	-3.60	-0.47	0.0112	0.0137
B-ALL vs Control	30	50	-0.40	-2.19	1.40	0.6626	0.7144
AML vs Control	7	50	-4.65	-6.96	-2.34	< 0.001	< 0.001
T-ALL vs Control	12	50	-3.54	-5.84	-1.24	0.0032	0.0293

β = adjusted regression coefficient (difference in mean $\log_2$ fold change, $-\Delta\Delta Ct$, vs. controls after age adjustment). Negative β values indicate downregulation relative to controls.
HC3 = heteroskedasticity-consistent robust standard errors.
n_{cases} denotes the number of patients included for each subtype comparison; $n_{controls}$ = 50 for all models.

and a group/subtype indicator as predictors, with miR-5192 $\Delta\Delta Ct$ as the outcome. The adjusted regression coefficient (β) represents the mean difference in $\Delta\Delta Ct$ between each leukemia group and controls after age adjustment; negative β values indicate lower expression (downregulation) relative to controls. Robust p-values (HC3) are also reported to account for potential heteroskedasticity. Here, n_{cases} denotes the number of patients included in each subtype comparison, and $n_{controls}$ = 50 for all models.

Age-adjusted, subtype-specific findings

miR-5192 expression differed across leukemia subtypes in age-adjusted subtype-specific models (Figure 2). B-ALL did not differ significantly from controls after age adjustment (Adjusted β = −0.40; 95% CI −2.19 to 1.40; p = 0.663; p_{robust} = 0.714). In contrast, AML showed marked downregulation relative to controls (Adjusted β = −4.65; 95% CI −6.96 to −2.34; p < 0.001; p_{robust} < 0.001), and T-ALL also demonstrated significant downregulation (Adjusted β = −3.54; 95% CI −5.84 to −1.24; p = 0.0032; p_{robust} = 0.029). Collectively, these findings suggest that miR-5192 downregulation is most pronounced in AML and T-ALL, whereas its role in B-ALL remains less clear. CML cases (n = 1; mean $\Delta\Delta Ct$ = −2.65) were excluded from age-adjusted analyses due to insufficient sample size.

In Figure 2, bars represent the age-adjusted regression coefficient (β) from subtype-specific ANCOVA/linear regression models including age (years) as a covariate and miR-5192 $\Delta\Delta Ct$ as the outcome. Each β estimates the mean difference in $\Delta\Delta Ct$ between the specified leukemia subtype and controls after age adjustment; negative β values indicate lower miR-5192 expression relative to controls. In this study, the adjusted effect was not significant for B-ALL vs. controls (β = −0.40), but was significantly negative for AML vs. controls (β = −4.65) and T-ALL vs. controls (β = −3.54), consistent with subtype-specific downregulation.

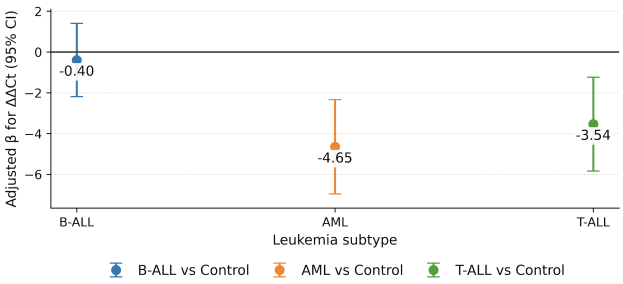

Figure 2. Age-adjusted subtype-specific effects on miR-5192 expression compared with controls (adjusted β for $\Delta\Delta Ct$ with 95% CI). Negative values indicate down-regulation relative to controls.

DISCUSSION

MicroRNAs (miRNAs) are key post-transcriptional regulators of gene expression and are implicated in cancer initiation and progression. Depending on the cellular context and their targets, miRNAs may function as tumor suppressors or oncogenes, and in some settings the same miRNA can exert dual roles across different tissues or disease stages. Because miRNAs are broadly expressed and participate in pathways controlling proliferation, differentiation, and apoptosis, their expression profiles are increasingly recognized as useful candidates for cancer diagnosis, classification, and risk stratification [13, 14].

Childhood leukemia exhibits age-related variation in incidence, with peaks reported in early childhood and again in later pediatric age groups, suggesting that age may influence disease susceptibility and presentation [15]. In the present study, most cases occurred in the 7–10-year age group, which is broadly consistent with regional Iraqi reports describing higher frequencies of pediatric leukemia between 2 and 10 years [16]. A slight male predominance was observed among cases, in agreement with previous studies indicating that childhood leukemia is more common in males than females [17, 18].

The principal finding of this study is that miR-5192 was significantly downregulated in leukemic children compared with controls (Table 4), supporting a potential tumor-suppressive role [19]. Published evidence on miR-5192 in pediatric leukemia is limited; this is the first report assessing miR-5192 expression in pediatric leukemia. Although direct mechanistic evidence for miR-5192 in leukemogenesis is currently limited, indirect support comes from observations on other miRNAs located on chromosome 2—including miR-22 and miR-192—which have been reported to be reduced in leukemia and implicated in pathways relevant to leukemic transformation and progression [20, 21]. Taken together, these findings provide preliminary biological plausibility for the association between miR-5192 downregulation and pediatric leukemia.

Importantly, subtype-specific analyses (Table 5) suggest heterogeneity in miR-5192 dysregulation across major leukemia subtypes. miR-5192 downregulation was most pronounced in AML and T-ALL, which aligns with the established concept of miRNA network disruption in these malignancies, where loss of inhibitory miRNAs can promote leukemic cell survival, impaired differentiation, and treatment resistance [22, 23]. Consistent with this framework, prior studies in pediatric AML have highlighted the biological and prognostic relevance of several miRNAs, including miR-192 and miR-381, emphasizing the importance of miRNA-mediated regulation in myeloid leukemogenesis [24, 25].

In T-ALL, NOTCH1-driven signaling and miRNA-dependent regulatory circuits are central to disease pathogenesis [26, 27]. Dysregulation of miRNAs affecting NOTCH1 and MYC-associated programs has been widely reported, and MYC is a major proto-oncogene that controls cell growth, proliferation, and apoptosis [28–30]. Although direct evidence linking miR-5192 to NOTCH1 signaling is not yet available, the observed downregulation of miR-5192 in T-ALL could hypothetically contribute to pro-leukemogenic signaling by reducing miRNA-mediated inhibitory control over relevant downstream targets. This interpretation remains speculative and underscores the need for functional studies to identify miR-5192 targets and to clarify its mechanistic role in T-ALL biology.

In contrast, miR-5192 expression was not significantly altered in B-ALL (Table 5). This finding may reflect subtype-specific molecular drivers in B-ALL, in which alternative oncogenic mechanisms—including CRLF2–JAK/STAT signaling and recurrent alterations in transcription factors such as *PAX5* and *IKZF1*—play dominant roles in leukemic proliferation and survival [31–33]. Moreover, B-ALL progression is strongly influenced by B-cell lineage-associated miRNAs (e.g., miR-181a and miR-155), which regulate differentiation and immune signaling and may overshadow the contribution of miR-5192 in this subtype [34]. Alternatively, miR-5192 may be more relevant to myeloid or T-lineage contexts, consistent with its stronger downregulation observed in AML and T-ALL.

Chronic myeloid leukemia (CML) was rare in our cohort and was excluded from age-adjusted analyses. This is consistent with epidemiological data indicating that CML accounts for only about 2–3% of childhood leukemias [35, 36].

This study has limitations. First, it was conducted at a single center with a modest sample size, limiting representation of individual subtypes (particularly AML) and reducing generalizability. Second, recruitment of healthy pediatric controls was challenging, resulting in incomplete age matching between groups and necessitating age-adjusted analyses. Third, control participants were assessed primarily by history and clinical evaluation; complete blood count (CBC) testing was not performed to objectively exclude subclinical hematologic abnormalities. Finally, because miR-5192 has been minimally studied in leukemia, interpretation relied partly on evidence from related miRNAs, which restricts direct comparison.

Despite these limitations, the present findings provide initial evidence that miR-5192 is downregulated in pediatric leukemia, with subtype-specific patterns suggesting stronger involvement in AML and T-ALL. Larger multicenter studies with well-matched controls are warranted to confirm these observations. In addition, mechanistic investigations are needed to identify miR-5192 target genes and pathways, and to evaluate whether modulation of miR-5192 could have diagnostic, prognostic, or therapeutic relevance in pediatric leukemia.

CONCLUSION

miR-5192 is significantly downregulated in pediatric leukemia compared with healthy controls, supporting a potential tumor-suppressive role in leukemogenesis. Downregulation is most pronounced in acute myeloid leukemia (AML) and T-acute lymphoblastic leukemia (T-ALL), whereas miR-5192 expression does not differ significantly in B-acute lymphoblastic leukemia (B-ALL), indicating subtype-specific variation. Validation in larger multicenter cohorts and functional studies is required to clarify the underlying mechanisms and to determine the diagnostic and prognostic value of miR-5192 as a biomarker in pediatric leukemia.

ETHICAL DECLARATIONS

Ethics Approval and Consent to Participate

Ethical approval was obtained from the College of Medicine, University of AL-Iraqia, Baghdad, Iraq (No. FM.SA/49), 24/4/2024. All participants provided consent, and they were assured that patient information would be kept confidential and secure throughout the study.

Consent for Publication

None.

Availability of Data and Material

The datasets are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that there is no conflict of interest.

Funding

Self-funded.

Use of Generative Artificial Intelligence

The authors declare that no generative AI tools were used in the preparation, writing, or editing of this manuscript.

Authors' Contributions

All authors contributed to the literature review, study design, data collection, statistical analysis, and manuscript preparation. All authors have read and approved the final version of the manuscript.

REFERENCES

[1] Munir F, He J, Connors J, Garcia M, Gibson A, McCall D, et al., Translational advances in the treatment of childhood acute lymphoblastic leukemia: narrative review of current and emerging molecular and immunotherapies. *Translational Pediatrics* 2023;12(3):487. https://doi.org/10.21037/tp-22-656

[2] Abdulridha R, Jawad N, Tariq AN, Prevalence and Risk of Leukemia Reported Cases, Observational Descriptive Statistic from Iraqi Center for Hematology in Baghdad Province. *Indian Journal of Forensic Medicine & Toxicology* 2021;15(1):2428–2433. https://doi.org/10.37506/ijfmt.v15i1.13765

[3] Elgazar S, Constantinou C, Paediatric Acute Lymphoblastic Leukaemia: A Narrative Review of Current Knowledge and Advancements. *Current Oncology Reports* 2024;26(12):1586–1599. https://doi.org/10.1007/s11912-024-01608-4

[4] Shang R, Lee S, Senavirathne G, Lai E, microRNAs in action: biogenesis, function and regulation. *Nature Reviews Genetics* 2023;24(12):816–833. https://doi.org/10.1038/s41576-023-00611-y

[5] Szczepanek J, Role of microRNA dysregulation in childhood acute leukemias: Diagnostics, monitoring and therapeutics: A comprehensive review. *World Journal of Clinical Oncology* 2020;11(6):348–369. https://doi.org/10.5306/wjco.v11.i6.348

[6] Sharma M, miRNA regulation in cancer progression: A molecular network review. *International Journal of Biological Sciences* 2024;6(1):193–203. https://doi.org/10.33545/26649926.2024.v6.i1c.429

[7] Turk A, Calin G, Kunej T, MicroRNAs in Leukemias: A Clinically Annotated Compendium. *International Journal of Molecular Sciences* 2022;23(7):3469. https://doi.org/10.3390/ijms23073469

[8] Mendiola-Soto D, Bárcenas-López D, Pérez-Amado C, Cruz-Miranda G, Mejía-Aranguré J, Ramírez-Bello J, et al., MiRNAs in Hematopoiesis and Acute Lymphoblastic Leukemia. *International Journal of Molecular Sciences* 2023;24(6):5436. https://doi.org/10.3390/ijms24065436

[9] Tsotridou E, Georgiou E, Tragiannidis A, Avgeros C, Tzimagiorgis G, Lambrou M, et al., miRNAs as predictive biomarkers of response to treatment in pediatric patients with acute lymphoblastic leukemia. *Oncology Letters* 2024;27(2). https://doi.org/10.3892/ol.2023.14204

[10] Mulet-Lazaro R, van Herk S, Nuetzel M, Sijs-Szabo A, Díaz N, Kelly K, et al., Epigenetic alterations affecting hematopoietic regulatory networks as drivers of mixed myeloid/lymphoid leukemia. *Nature Communications* 2024;15(1):5693. https://doi.org/10.1038/s41467-024-49811-y

[11] Jang J, Lee T, The role of microRNAs in cell death pathways. *Yeungnam University Journal of Medicine* 2021;38(2):107–177. https://doi.org/10.12701/yujm.2020.00836

[12] Livak KJ, Schmittgen TD, Analysis of Relative Gene Expression Data Using Real-Time Quantitative PCR and the 2ΔΔCT Method. *Methods* 2001;25(4):402–408. https://doi.org/10.1006/meth.2001.1262

[13] Otmani K, Lewalle P, Tumor Suppressor miRNA in Cancer Cells and the Tumor Microenvironment: Mechanism of Deregulation and Clinical Implications. *Frontiers in Oncology* 2021;11:708765. https://doi.org/10.3389/fonc.2021.708765

[14] Condrat CE, Thompson DC, Barbu MG, Bugnar OL, Boboc A, Cretoiu D, et al., MiRNAs as Biomarkers in Disease: Latest Findings Regarding Their Role in Diagnosis and Prognosis. *Cells* 2020;9(2):276. https://doi.org/10.3390/cells9020276

[15] Cui Y, Yan Y, The global burden of childhood and adolescent leukaemia and attributable risk factors: An analysis of the Global Burden of Disease Study 2019. *Journal of Global Health* 2024;14:04045. https://doi.org/10.7189/jogh.14.04045

[16] Anwer A, Demographic and pattern of childhood acute leukemia in Duhok, Kurdistan region of Iraq, 2009-2018. *Advanced Medical Journal* 2020;6(1):22–27. https://doi.org/10.56056/amj.2020.114

[17] AL-Saidi DN, Role of Age and Sex on the Incidence of Leukemia in a Sample of Iraqi Patients. *Medical Journal of Babylon* 2024;21(Suppl 2):S229–S233. https://doi.org/10.4103/MJBL.MJBL_929_23

[18] De-Morgan A, Meggendorfer M, Haferlach C, Shlush L, Male predominance in AML is associated with specific preleukemic mutations. *Leukemia* 2021;35(3):867–870. https://doi.org/10.1038/s41375-020-0935-5

[19] Menon A, Abd-Aziz N, Khalid K, Poh CL, Naidu R, miRNA: A Promising Therapeutic Target in Cancer. *International Journal of Molecular Sciences* 2022;23(19):11502. https://doi.org/10.3390/ijms231911502

[20] Xia J, Bu C, Zhang B, Wang X, Chen Y, Li T, The emerging role of microRNA-22 in leukemia: experimental and clinical implications. *Molecular Biology Reports* 2023;51(1):12. https://doi.org/10.1007/s11033-023-08922-3

[21] Tian C, Zhang L, Li X, Zhang Y, Li J, Chen L, Low miR-192 expression predicts poor prognosis in pediatric acute myeloid leukemia. *Cancer Biomarkers* 2018;22(2):209–215. https://doi.org/10.3233/CBM-170657

[22] Wiśnik A, Jarych D, Krawiec K, Strzałka P, Potocka N, Czemerska M, et al., Role of microRNAs in acute myeloid leukemia. *Genes* 2025 Apr;16(4):446. https://doi.org/10.3390/genes16040446

[23] Stubbins RJ, Karsan A, Differentiation therapy for myeloid malignancies: Beyond cytotoxicity. *Blood Cancer Journal* 2021;11(12):193. https://doi.org/10.1038/s41408-021-00584-3

[24] Ellson I, Martorell-Marugán J, Carmona-Sáez P, Ramos-Mejía V, MiRNA expression as outcome predictor in pediatric AML: systematic evaluation of a new model. *npj Genomic Medicine* 2024;9(1):40. https://doi.org/10.1038/s41525-024-00424-w

[25] Zhang P, Sun D, Sun X, Li H, Clinical significance of dysregulation of miR-381 in pediatric acute myeloid leukemia. *European Journal of Medical Research* 2020;25(1). https://doi.org/10.1186/s40001-020-00442-1

[26] Sergio I, Varricchio C, Squillante F, Cantale AN, Campese A, Felli M, Notch inhibitors and BH3 mimetics in T-cell acute lymphoblastic leukemia. *International Journal of Molecular Sciences* 2024;25(23):12839. https://doi.org/10.3390/ijms252312839

[27] Colangelo T, Panelli P, Mazzarelli F, Tamiro F, Melocchi V, De Santis E, et al., Extracellular vesicle microRNAs contribute to Notch signaling pathway in T-cell acute lymphoblastic leukemia. *Molecular Cancer* 2022;21(1):226. https://doi.org/10.1186/s12943-022-01698-3

[28] Gębarowska K, Mroczek A, Kowalczyk JR, Lejman M, MicroRNA as a prognostic and diagnostic marker in T-cell acute lymphoblastic leukemia. *International Journal of Molecular Sciences* 2021;22(10):5317. https://doi.org/10.3390/ijms22105317

[29] Dhanasekaran R, Deutzmann A, Mahauad-Fernandez WD, Hansen AS, Gouw AM, Felsher DW, The MYC oncogene - the grand orchestrator of cancer growth and immune evasion. *nature reviews clinical oncology* 2022;19(1):23–36. https://doi.org/10.1038/s41571-021-00549-2

[30] Li Q, Pan S, Xie T, Liu H, MYC in T-cell acute lymphoblastic leukemia: Functional implications and targeted strategies. *Blood Science* 2021;3(3):65–70. https://doi.org/10.1097/BS9.0000000000000073

[31] Østergaard A, Boer JM, van Leeuwen FN, Pieters R, Den Boer ML, IKZF1 in acute lymphoblastic leukemia: The rise before the fall? *Leukemia & Lymphoma* 2024;65(14):1–11. https://doi.org/10.1080/10428194.2024.2396046

[32] Maciel ALT, Barbosa TDC, Blunck CB, Wolch K, Machado AAL, da Costa ES, et al., IKZF1 deletions associate with CRLF2 overexpression leading to a poor prognosis in B-cell precursor acute lymphoblastic leukaemia. *Translational Oncology* 2022;15(1):101291. https://doi.org/10.1016/j.tranon.2021.101291

[33] Roberts KG, Mullighan CG, The Biology of B-Progenitor Acute Lymphoblastic Leukemia. *Cold Spring Harbor Perspectives in Medicine* 2019;10(7):a034835. https://doi.org/10.1101/cshperspect.a034835

[34] Dhiflaoui A, Almawi WY, Mechanisms and clinical implications of microRNA associations and signaling pathways in B-cell acute lymphoblastic leukemia. *Gene* 2025;967:149730. https://doi.org/10.1016/j.gene.2025.149730

[35] Athale U, Hijiya N, Patterson BC, Bergsagel J, Andolina JR, Bittencourt H, et al., Management of chronic myeloid leukemia in children and adolescents: Recommendations from the Children's Oncology Group CML Working Group. *Pediatric Blood & Cancer* 2019;66(9):e27827. https://doi.org/10.1002/pbc.27827

[36] Karow A, Göhring G, Sembill S, Lutterloh F, Neuhaus F, Callies S, et al., The Cytogenetic Landscape of Pediatric Chronic Myeloid Leukemia Diagnosed in Chronic Phase. *Cancers* 2022;14(7):1712. https://doi.org/10.3390/cancers14071712