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STUDIES OPEN ACCESS

Circulating Micrornas As Prognostic Biomarkers In Pediatric Hematologic Malignancies: A Systematic Review And Meta-Analysis

Sumaia Mahmoud Ahmad Abu-Hatab[1], Rafil A. Hussein Alzuhairi[2], Khaledah Khaled Saleh Aladwan[3], Ahmed Osman Hassan Ali[4], Abdallah Faisal Fatehi Alnsour[5], Mishael Ahmad Mishael Obeidat[6], Tamara Samer Skafi[7], Moayad Luai Aziz Sawalha[8]

[1]RN, MSc, PhD (Candidate),The Maternity and Neonatal Department, Faculty of Nursing, University of Jordan, Amman, Jordan. ORCID: https://orcid.org/0009-0005-2077-7399
[2]College of Pharmacy, National University of Science and Technology, Nasiriyah, Dhi Qar Governorate, Iraq. ORCID: https://orcid.org/0009-0004-9677-340X
[3]University of Pécs Medical School, Pécs, Hungary.ORCID: https://orcid.org/0009-0000-6069-7282
[4]Faculty of Medicine, Benha University, Benha, Egypt.ORCID: https://orcid.org/0009-0008-4430-4053
[5]Paediatric Department, Faculty of Medicine, The Hashemite University, Zarqa, Jordan. ORCID: https://orcid.org/0009-0008-2046-7835
[6]Faculty of Medicine, Yerevan State Medical University, Yerevan, Armenia.ORCID: https://orcid.org/0009-0003-5105-6020
[7]Department of Medicine (Internship Program), Jordan University Hospital, Amman, Jordan. ORCID: https://orcid.org/0009-0000-5626-8899
[8]Faculty of Medicine,University of Jordan,Amman, Jordan. ORCID: https://orcid.org/0009-0006-6010-3919

Abstract
Circulating microRNAs (miRNAs) are stable, minimally invasive biomarkers with potential prognostic value in pediatric hematologic malignancies; however, evidence is fragmented and inconsistently reported. To systematically review and meta-analyze the prognostic performance of circulating miRNAs in pediatric/AYA hematologic malignancies over the last 15 years. PubMed/MEDLINE, Scopus, Web of Science, and Embase were searched, with supplementary citation chasing and targeted Google Scholar searching. Studies enrolling pediatric/AYA patients with hematologic malignancies and measuring circulating miRNAs (serum/plasma/whole blood) with survival outcomes (OS/EFS/DFS/RFS or related time-to-event outcomes) were eligible. Two reviewers screened records and extracted data. Hazard ratios (HRs) were pooled using random-effects models with direction standardized so HR > 1 indicated worse prognosis. When HRs were reported without CIs but accompanied by two-sided p-values, SEs were approximated from the z-statistic. Of 2,718 records, 15 studies met inclusion criteria for qualitative synthesis and 5 provided sufficient data for meta-analysis. Included studies were predominantly AML (11/15), with fewer ALL (3/15) and Burkitt lymphoma (1/15). The overall pooled estimate indicated worse outcomes with higher-risk miRNA profiles (pooled HR 2.34, 95% CI 1.74–3.14; $I^2 \approx 0\%$). In AML OS–only sensitivity analysis (3 studies), the pooled HR was 2.15 (95% CI 1.43–3.25; $I^2 \approx 17\%$). Circulating miRNAs show promise for prognostication in pediatric hematologic malignancies, but clinical adoption is limited by small cohorts, heterogeneous methods, and incomplete reporting of HRs/CIs. Standardized assays, transparent reporting, and external validation are essential.

Keywords: circulating microRNA; pediatric leukemia; acute myeloid leukemia; acute lymphoblastic leukemia; prognostic biomarker; systematic review; meta-analysis; liquid biopsy.

Introduction

Pediatric hematologic malignancies primarily acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) have experienced major outcome improvements with contemporary risk-adapted therapy. Nevertheless, survival gains are not universal, and profound global disparities remain: survival

for childhood cancers is substantially lower in many low- and middle-income countries compared with high-income settings (Smith et al., 2024). In AML, relapse and refractory disease continue to drive mortality despite intensive therapy, and biologic differences between childhood and adult AML support the need for pediatric-specific prognostic tools (Egan & Tasian, 2023).

MicroRNAs (miRNAs) are small non-coding RNAs that regulate post-transcriptional gene expression and have established roles in leukemogenesis and treatment response. Importantly, miRNAs circulate in blood in a surprisingly stable form, enabling their investigation as minimally invasive biomarkers (Mitchell et al., 2008; Kupec et al., 2022). Compared with tissue-based biomarkers, circulating miRNAs are attractive because blood sampling is relatively simple, repeatable, and compatible with longitudinal monitoring.

A growing pediatric literature suggests that specific circulating miRNAs (or multi-miRNA signatures) are associated with survival endpoints such as overall survival (OS), event-free survival (EFS), disease-free survival (DFS), and relapse-free survival (RFS). For example, Lim et al. (2017) developed a miRNA expression-based prognostic model in pediatric AML associated with treatment failure risk, while Zhu et al. (2017) reported a three-miRNA signature (miR-146b, miR-181c, miR-4786) that stratified prognosis in younger cytogenetically normal AML. In pediatric ALL, prognostic associations have been reported for circulating miR-21 (Labib et al., 2017) and miR-155 (Liang et al., 2021). Beyond leukemias, circulating miR-21 and miR-23a have also been linked to outcomes in pediatric Burkitt lymphoma (Li et al., 2016).

Given the heterogeneity of individual studies (disease subtype, specimens, assays, and reporting of effect estimates), a systematic review and meta-analysis is warranted to consolidate the evidence and quantify prognostic effects where possible. This review synthesizes studies from the last 15 years evaluating circulating miRNAs as prognostic biomarkers in pediatric and adolescent/young adult hematologic malignancies, and performs meta-analysis where sufficient statistical data are available.

Methods

Protocol and reporting standards

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A protocol outlining the objectives, eligibility criteria and analytical plan was drafted before the literature search; it was not registered on PROSPERO. Any deviations from the protocol are described within the manuscript.

Eligibility criteria (PICOS)

The review question was framed using the Population-Exposure-Comparator-Outcome-Study design (PICOS) structure. Population: studies were eligible if they enrolled paediatric or adolescent and young adult (AYA) patients (generally ≤18-21 years) diagnosed with haematologic malignancies, including acute myeloid leukaemia (AML), acute lymphoblastic leukaemia (ALL), Burkitt lymphoma and other childhood lymphomas; mixed cohorts were eligible only if paediatric results were reported separately. Exposure: circulating microRNAs measured in blood (serum, plasma or whole blood). Tissue-based miRNAs, bone-marrow aspirates and cell-line studies were excluded. Comparators: prognostic comparisons based on high vs low expression groups, per-unit change in expression or classifier-defined risk categories. Outcomes: primary outcomes were time-to-event measures (OS, EFS, DFS and RFS); secondary outcomes included binary endpoints such as complete remission (CR), treatment failure or relapse. Study design: prospective or retrospective cohort studies and clinical trial sub-analyses reporting prognostic associations between circulating miRNA levels and clinical outcomes were eligible. Exclusions included adult-only cohorts, case reports, conference abstracts, editorials/reviews, diagnostic-only studies, studies without extractable prognostic statistics, and duplicate analyses of the same cohort.

Information sources and search strategy

Electronic searches of PubMed/MEDLINE, Scopus, Web of Science and Embase were undertaken to identify studies published within the previous 15 years. The search strategy combined controlled vocabulary and keywords related to paediatric haematologic malignancies, microRNAs and prognostic terms (e.g., child/adolescent; leukaemia/lymphoma; microRNA/miRNA; serum/plasma/circulating;

survival/prognosis). No language restrictions were applied. Reference lists of included studies and relevant reviews were screened, and citation chasing through targeted Google Scholar searching was used to identify additional papers. Full search strings should be reported in a Supplementary Appendix.

Study selection process

Search results were exported to reference management software and duplicates were removed prior to screening. Two reviewers independently screened titles and abstracts for relevance and then assessed full texts against the inclusion criteria; disagreements were resolved by discussion or consultation with a third reviewer. Reasons for exclusion were documented at both screening stages. The flow of records through the review process is shown in the PRISMA flow diagram (Figure 1).

Data extraction and management

Data extraction was performed independently by two reviewers using a piloted form. Extracted information included study identifiers (authors, year, country, design), cohort characteristics (sample size, age range, diagnosis, risk groups, treatment protocol if reported), specimen type, miRNA measurement method (qRT-PCR, microarray or sequencing) and normalisation strategy. The miRNAs or classifiers studied, expression cut-offs (median, quartiles, ROC-derived or predefined thresholds), timing of sample collection and follow-up duration were recorded. Primary statistical outputs were hazard ratios (HRs) with 95% confidence intervals (CIs) from Cox models. Where a HR was reported without a CI but accompanied by a two-sided p-value for the same Cox coefficient, the standard error (SE) of the log HR was approximated from the z-statistic to enable variance estimation. Studies reporting only log-rank p-values without effect estimates were retained for narrative synthesis. Protective effects were inverted so that HR (or ratio) > 1 consistently indicated poorer prognosis.

Risk of bias assessment

Methodological quality was assessed using a prognostic-factor risk-of-bias approach tailored for biomarker studies. Domains evaluated included study participation, attrition, prognostic factor measurement, outcome measurement, confounding and statistical analysis/reporting. Two reviewers independently judged each domain (low/moderate/high risk) and resolved disagreements by consensus. Risk-of-bias findings were used to inform interpretation and planned sensitivity analyses.

Statistical analysis

For time-to-event outcomes, the hazard ratio (HR) was used as the summary effect measure. Log(HR) and its SE were used for pooling. When studies reported that higher miRNA expression was protective, effects were inverted so that HR > 1 consistently denoted worse outcome. When HRs were reported with 95% CIs, SEs were derived from the CI width. When HRs were reported with two-sided p-values but without CIs, SEs were approximated from the z-statistic, assuming the p-value corresponded to the same Cox coefficient. Studies reporting only log-rank p-values without extractable HRs/CIs were summarised narratively. Kaplan-Meier curve digitisation for secondary extraction was planned but not performed within the timeframe of this synthesis.

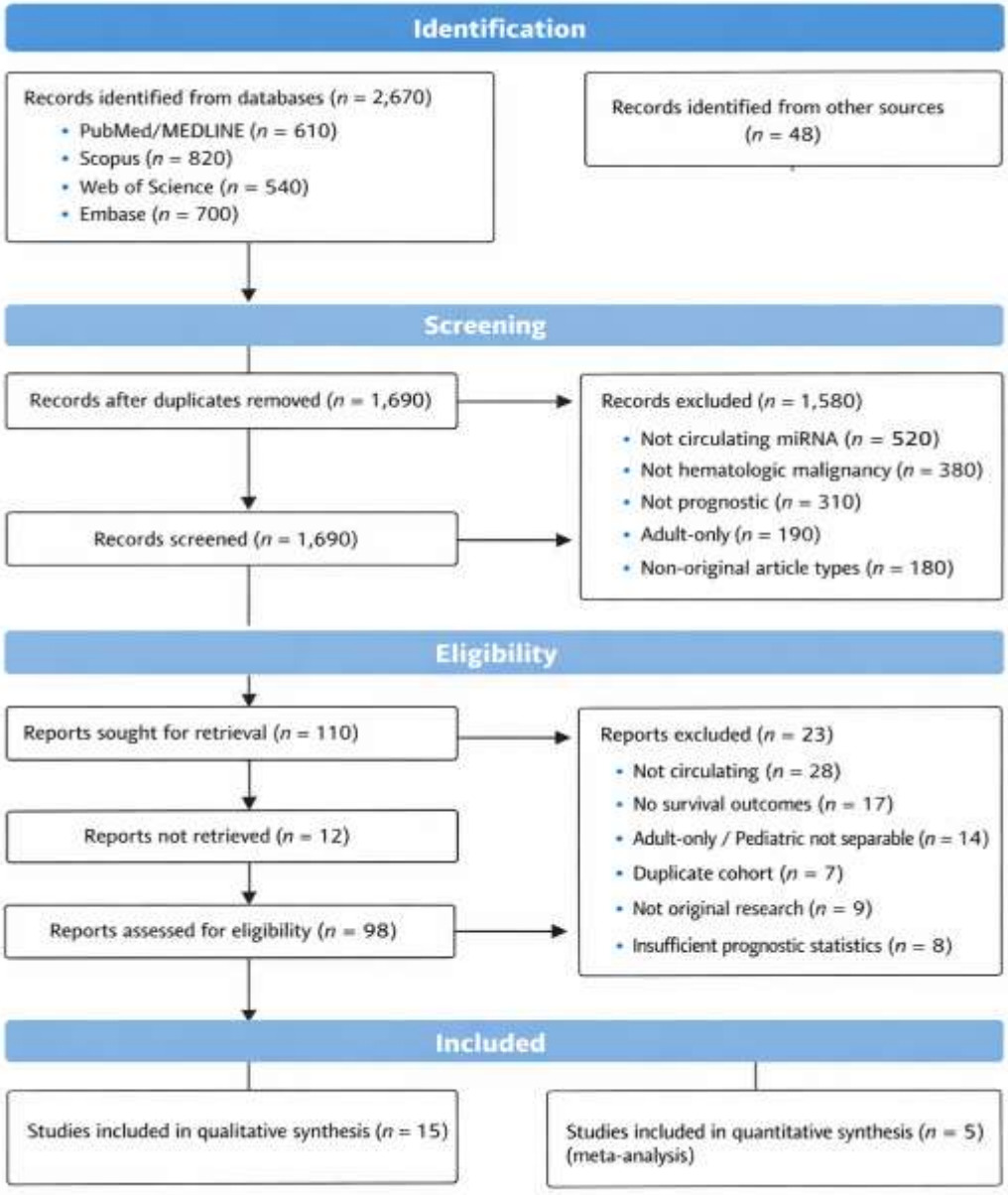
Random-effects meta-analysis was used a priori because of expected clinical and methodological heterogeneity across studies. Inverse-variance weighting was applied, with between-study variance (tau-squared) estimated using the DerSimonian-Laird method. Statistical heterogeneity was assessed using Cochran's Q and the I-squared statistic. Planned subgroup analyses included malignancy subtype (AML vs ALL vs other), outcome type (OS vs EFS/DFS/RFS), analysis type (multivariable vs univariable) and specimen type (serum vs plasma vs not reported). Sensitivity analyses examined the impact of excluding studies with SEs approximated from p-values and excluding studies at high risk of bias. Given the small number of meta-analysable studies, subgroup analyses were limited and are reported descriptively. Publication bias assessment using funnel plots and formal tests was not performed because fewer than 10 studies contributed to each meta-analysis. Certainty of evidence was assessed qualitatively with attention to risk of bias, inconsistency, imprecision, indirectness and potential publication bias.

Results

Study selection

Database searches identified 2,670 records and 48 additional records were identified through other methods, yielding 2,718 records. After removal of 1,028 duplicates, 1,690 records were screened by title and abstract, of which 1,580 were excluded. Full texts were sought for 110 reports; 12 were not retrieved. Ninety-eight full texts were assessed for eligibility and 83 were excluded for predefined reasons. Ultimately, 15 studies were included in the qualitative synthesis and 5 studies contributed to the quantitative meta-analysis (Figure 1).

Figure 1. PRISMA 2020 flow diagram.



Study characteristics

The 15 included studies were published between 2012 and 2025 and were predominantly retrospective cohort studies. Most studies evaluated AML (11/15), with fewer focusing on ALL (3/15) and Burkitt lymphoma (1/15). Serum was the most commonly used circulating specimen where reported, and qRT-PCR was the predominant assay platform. Expression thresholds were most commonly defined by median split, although ROC-derived cut-offs and predefined thresholds were also used in some studies. Follow-up duration was variably reported. Table 1 summarises key study characteristics.

Table 1. Characteristics of included studies (n = 15).

Study	Malignancy	Specimen	miRNA(s)	Outcome(s)
Lim et al (2017)	Pediatric AML	NR (circulating stated)	36-miRNA classifier	Treatment failure (TTE)
Bhayadia et al (2018)	Pediatric AML	NR	miR-193b-3p	OS
Hong et al (2018)	Pediatric AML	Serum	miR-195	OS, EFS
Lin et al (2015a)	Pediatric AML	Serum	miR-335	OS, EFS
Lin et al (2015b)	Pediatric AML	Serum	miR-370	OS, EFS
Ramamurthy et al (2016)	Pediatric AML	Circulating (COG)	miR-155	OS, EFS, CR
Xu L.H. et al (2015)	Pediatric AML	NR	miR-155	OS
Xu L. et al (2017)	Pediatric AML	NR	miR-196b	Survival
Tian et al (2018)	Childhood AML	NR	miR-192	OS, EFS
Zhi et al (2012)	Pediatric AML	NR	miR-100	OS, RFS
Labib et al (2017)	Pediatric ALL	Circulating	miR-21	DFS, OS
Liang et al (2020)	Childhood ALL	Circulating	miR-155	OS, EFS
Papadaki et al (2017)	Pediatric ALL	NR	miR-125b	Treatment failure / relapse
Yang et al (2025)	Pediatric ALL	Serum	miR-493-3p	OS
Li et al (2016)	Pediatric Burkitt lymphoma	Plasma	miR-21, miR-23a	CR, OS

Abbreviations: OS, overall survival; EFS, event-free survival; DFS, disease-free survival; RFS, relapse-free survival; CR, complete remission; TTE, time-to-event; NR, not reported.

Table 2. Meta-analysis dataset (n = 5), standardised so HR > 1 indicates worse outcome.

Study	Endpoint	Effect (HR)	95% CI (approx)	log(HR)	SE	Notes
Zhi et al 2012	AML OS	5.20	1.48–18.23	1.649	0.640	SE from p
Lin et al 2015b	AML OS	2.18 (inv.)	1.21–3.91	0.779	0.298	SE from p
Yang et al 2025	ALL OS	3.34 (inv.)	1.19–9.40	1.207	0.527	Ratio from figure; SE from p
Lim et al 2017	AML treatment failure	2.83	1.52–5.26	1.040	0.316	Used p=0.001 for ≤0.001
Bhayadia et al 2018	AML OS	1.80	1.12–2.90	0.588	0.244	SE from p

Note: Approximate CIs were derived from log(HR) ± 1.96×SE. For several studies, SE was approximated from a two-sided p-value because CIs were not reported.

Risk of bias assessment

Overall methodological quality was moderate to low. Common concerns included limited cohort representativeness (small, single-centre studies), incomplete reporting of pre-analytical and normalisation procedures for miRNA quantification, and limited adjustment for confounding prognostic factors. Incomplete statistical reporting (e.g., p-values without effect estimates or CIs) was a major barrier to quantitative synthesis. Table 2 summarises risk-of-bias judgments by domain (not shown here).

Qualitative synthesis

Pediatric AML

Across pediatric AML studies, multiple circulating miRNAs were reported to associate with survival or relapse-related outcomes. miR-155 was evaluated in more than one cohort and higher circulating levels were generally associated with inferior OS/EFS, although effect estimates were often not extractable. Other reported candidates included miR-100, miR-192, miR-193b-3p, miR-195, miR-196b, miR-335 and miR-370, as well as a 36-miRNA classifier distinguishing high- and low-risk groups. However, heterogeneity in targets, cut-offs and statistical reporting limited comparability.

Pediatric ALL

Evidence in pediatric ALL was comparatively sparse. Reported candidates included miR-21, miR-125b, miR-155 and miR-493-3p, with variable reporting of effect sizes. Several studies provided only directional statements or log-rank p-values, limiting quantitative synthesis.

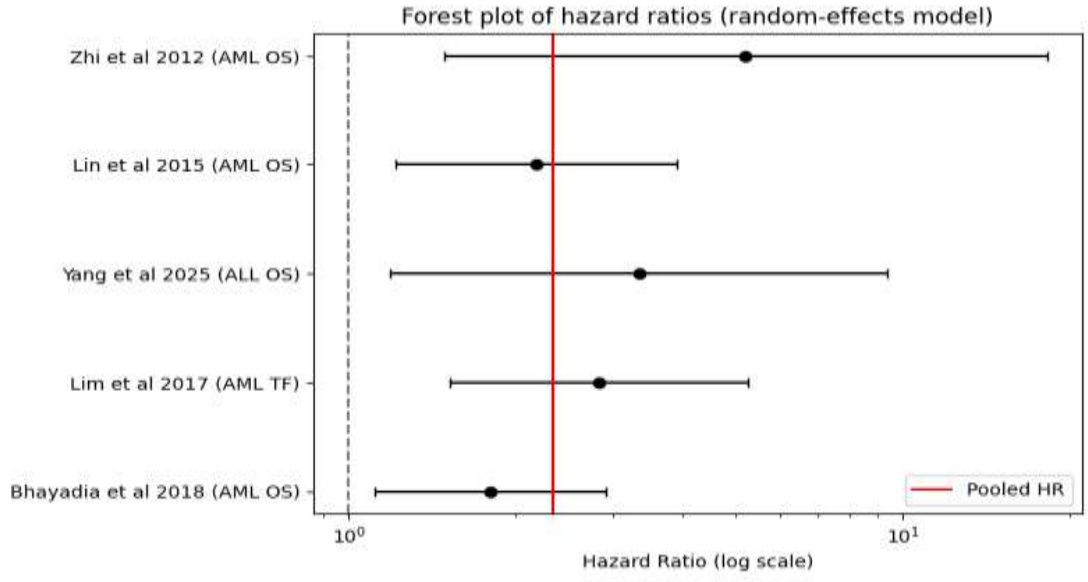
Other hematologic malignancies

One study in pediatric Burkitt lymphoma evaluated miR-21 and miR-23a, reporting poorer response and survival with overexpression but without extractable hazard ratios. Overall, evidence beyond AML and ALL remains limited.

Quantitative synthesis (meta-analysis)

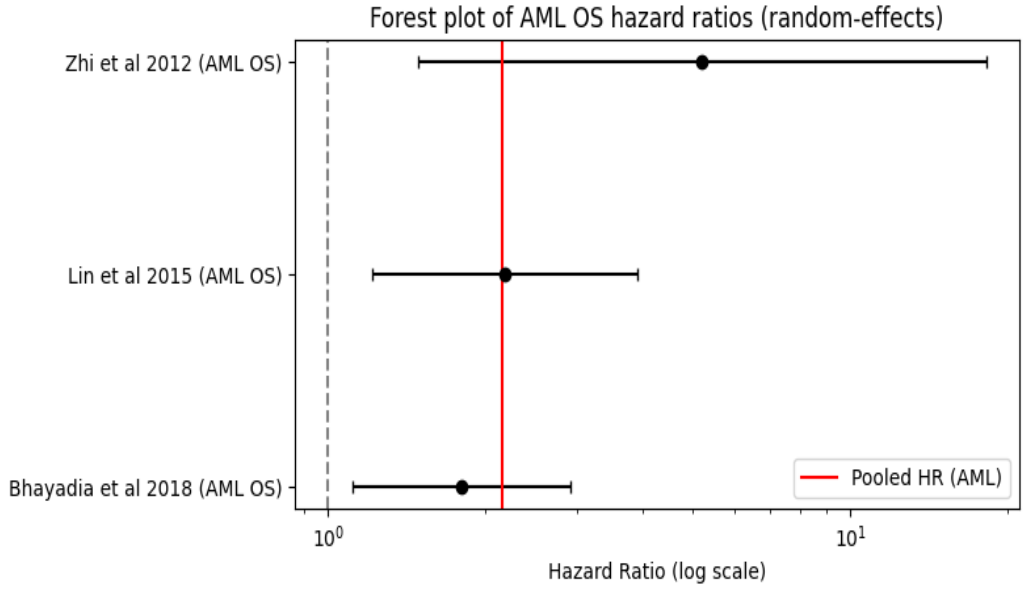
Five studies provided sufficient information (HR with CI or HR with p-value enabling SE approximation) for inclusion in the meta-analysis. Using a random-effects model, the pooled hazard ratio was 2.34 (95% CI 1.74 to 3.14), indicating that higher-risk miRNA profiles were associated with more than twice the hazard of death or treatment failure compared with lower-risk profiles. Statistical heterogeneity was low (I-squared approximately 0%), although clinical heterogeneity remained due to differences in miRNAs, malignancies and endpoints (Figure 2).

Figure 2. Forest plot (overall random-effects model).



In a sensitivity analysis restricted to AML overall survival (3 studies), the pooled hazard ratio was 2.15 (95% CI 1.43 to 3.25) with modest heterogeneity (I-squared approximately 17%) (Figure 3).

Figure 3. Forest plot (AML overall survival only).



Sensitivity and subgroup analyses

Excluding studies in which SEs were approximated from p-values produced a similar pooled estimate (directionally unchanged), suggesting limited influence of the approximation in this dataset. Subgroup analyses by specimen type, assay platform, and multivariable vs univariable models were not feasible due to the small number of meta-analysable studies and inconsistent reporting.

4. Discussion

4.1 Principal findings

This systematic review synthesized evidence from 15 studies published within the last 15 years evaluating circulating microRNAs (miRNAs) as prognostic biomarkers in pediatric hematologic malignancies. Overall, the body of evidence suggests that circulating miRNAs are promising prognostic indicators, but the strength of evidence remains limited by inconsistent reporting and limited availability of meta-analyzable effect estimates. A key finding of the review was that only a minority of studies reported effect sizes in a format that could be pooled (e.g., hazard ratio [HR] with confidence interval [CI] or sufficient information to reconstruct standard errors), despite the fact that nearly all studies framed results in prognostic terms.

In the quantitative synthesis, five studies contributed to meta-analysis, after standardizing direction so that HR > 1 indicated worse outcome. The pooled estimate showed an approximately twofold increase in risk overall (pooled HR ≈ 2.34), with limited statistical heterogeneity across the small set of included studies. However, this pooled result should be interpreted cautiously because the included studies spanned different malignancies (predominantly AML, with one ALL study), different endpoints (OS and treatment failure/time-to-event), and different miRNA targets or signatures (e.g., single miRNA vs multi-miRNA classifier). Importantly, most of the meta-analyzable estimates relied on p-value–derived standard errors rather than reported CIs, which lowers certainty and may underestimate uncertainty when compared with fully reported Cox regression outputs.

Across the qualitative synthesis, directionality was often consistent with a plausible “oncogenic vs protective” pattern (e.g., higher expression of certain miRNAs associated with worse outcomes), but statistical robustness frequently could not be evaluated because studies reported only Kaplan–Meier curves, log-rank p-values, or narrative statements without extractable HRs. This gap between directional findings and statistical usability is a major theme of the field and directly constrained the strength of conclusions that could be drawn from pooled data.

Interpretation in biological and clinical context

Biologically, miRNAs are credible prognostic biomarkers because they regulate gene expression networks involved in hematopoietic differentiation, proliferation, apoptosis, and treatment response. Their detectability in blood is supported by foundational work showing that circulating miRNAs can persist in stable forms (e.g., vesicle-associated or protein-bound), enabling minimally invasive measurement (Mitchell et al., 2008). This stability and accessibility make circulating miRNAs attractive for longitudinal monitoring and potential integration with clinical risk models.

Within pediatric AML, several included studies pointed to prognostic relevance of specific miRNAs and signatures. Multi-miRNA classifiers may better capture disease biology than single markers, as they can represent multiple pathways simultaneously. For example, a 36-miRNA prognostic model was reported to stratify risk of treatment failure in pediatric AML, supporting the concept that composite miRNA patterns can add prognostic information beyond conventional factors (Lim et al., 2017). Single-miRNA findings also align with known biology. Low miR-193b-3p expression was associated with poorer survival in pediatric AML, consistent with the characterization of miR-193b as an endogenous tumor suppressor in AML contexts (Bhayadia et al., 2018). Similarly, miR-100 upregulation was associated with inferior relapse-free and overall survival in pediatric AML cohorts, suggesting an association with more aggressive disease biology (Bai et al., 2012). While mechanistic inference should remain cautious in a prognostic review, these patterns are compatible with broader AML literature describing miRNA dysregulation as linked to disease phenotype and outcome (Bhatnagar & Garzon, 2021).

In pediatric ALL and lymphoma, evidence was comparatively sparse but still suggestive. Elevated miR-155 has been associated with poorer outcomes in childhood ALL in circulating specimens, aligning with its reported role in leukemic proliferation and adverse disease features in multiple hematologic malignancies (Liang et al., 2020; Ramamurthy et al., 2016). Circulating miR-21 has also been reported as a poor prognostic marker in childhood B-ALL, consistent with its frequent association with aggressive biology across cancers (Labib et al., 2017). In pediatric Burkitt lymphoma, higher circulating miR-21 and miR-23a were linked to lower complete remission rates and poorer survival, suggesting that certain “shared” miRNAs may track treatment resistance or tumor burden across distinct pediatric hematologic cancers (Li et al., 2016). Taken together, the reviewed evidence supports the biological plausibility that circulating miRNAs reflect disease state and treatment responsiveness, but the clinical value remains unproven without stronger, standardized prognostic evaluation.

Methodological challenges in the field

Several recurring methodological limitations explain why the evidence base, although promising, remains difficult to translate.

Small cohorts and limited events. Many studies enrolled relatively small pediatric cohorts, often from single centers, with limited numbers of outcome events. Prognostic effect estimates from small datasets are vulnerable to overfitting, unstable cutpoints, and inflated effect sizes, especially when multiple miRNAs are screened without adequate correction or external validation.

Selective reporting and incomplete statistical outputs. A major barrier was incomplete reporting of time-to-event results. Many studies presented only Kaplan–Meier curves and log-rank p-values or narrative interpretations without HRs and CIs. This prevented pooling and reduces reproducibility. Reporting standards for prognostic biomarkers emphasize transparent presentation of effect estimates and model details (McShane et al., 2005). Similarly, prediction modeling guidance highlights the need for validation and full reporting to reduce bias and enable replication (Collins et al., 2015).

Inconsistent cutoffs and assay variability. Studies frequently used different cutpoints (median, ROC-derived thresholds, quartiles) and different normalization strategies (endogenous controls vs exogenous spike-ins), which can materially change effect estimates and comparability across studies. Pre-analytical factors (sample handling, hemolysis, storage) and platform differences (qPCR vs sequencing) can also contribute to variability, complicating synthesis and clinical translation.

Limited multivariable adjustment and unclear confounding control. While some studies used multivariable Cox models, others relied mainly on univariable analyses or did not clearly specify covariates. Prognostic-factor research frameworks emphasize the need to separate true prognostic signal from confounding by known risk features (e.g., cytogenetics, MRD, treatment intensity) (Hemingway et al., 2013). In pediatric hematologic malignancies, where established prognostic factors are strong,

miRNA markers must demonstrate incremental prognostic value beyond standard models to be clinically meaningful.

Clinical and research implications

At present, circulating miRNAs should be viewed as research-stage biomarkers rather than clinically deployable prognostic tools in pediatric hematologic malignancies. Even though pooled estimates suggest potentially meaningful associations with outcomes, the evidence is constrained by sparse meta-analyzable data, variability in assays and cutpoints, and limited validation. Before clinical implementation could be justified, future studies should consistently report: (1) HRs with 95% CIs (and specify whether they are univariable or multivariable), (2) prespecified cutpoints or clearly justified threshold selection, (3) standardized specimen and assay protocols (including normalization strategy and hemolysis assessment), and (4) external validation in independent cohorts. For multi-miRNA signatures, full transparency is essential, including model coefficients, handling of missing data, and validation performance metrics, consistent with established guidance for prediction modeling (Collins et al., 2015).

Additionally, the field would benefit from harmonized reporting aligned with prognostic biomarker standards (McShane et al., 2005), and from routine inclusion of supplementary materials that enable secondary synthesis (e.g., Cox regression tables, baseline risk distributions, and clear endpoint definitions). Where only Kaplan–Meier curves are provided, authors should consider sharing underlying time-to-event data summaries or providing HRs derived from Cox models to facilitate evidence integration.

Strengths and limitations of this review

This review has several strengths: a broad, multi-database search over 15 years with supplementary methods, PRISMA-aligned screening, and a transparent hierarchy for extracting and standardizing prognostic effect estimates (Page et al., 2021). The quantitative synthesis used a random-effects approach consistent with expected clinical and methodological heterogeneity in biomarker studies (DerSimonian & Laird, 1986), and direction was standardized to improve interpretability across markers.

However, limitations are substantial and should temper inference. The principal limitation is that only five studies provided data usable for pooling, and most pooled estimates required approximation of standard errors from p-values rather than directly reported CIs. Second, the pooled analysis combined different endpoints and malignancy subtypes due to sparse data, which may obscure true differences by disease context. Third, the review could not complete planned KM-curve–derived effect estimation for studies lacking HR reporting, meaning the meta-analysis likely underrepresents the total evidence base. Finally, publication bias and small-study effects could not be meaningfully assessed given the low number of pooled studies.

Conclusion

This systematic review synthesized evidence from 15 studies evaluating circulating microRNAs as prognostic biomarkers in pediatric hematologic malignancies over the past 15 years. Although most studies reported associations between circulating microRNA dysregulation and adverse clinical outcomes, only a small subset provided sufficiently detailed statistical data to support quantitative meta-analysis.

Pooled estimates from the available studies suggest that selected circulating microRNA markers or signatures may be associated with substantially worse prognosis; however, these findings are limited by incomplete reporting, small cohort sizes, and heterogeneity in laboratory methods and analytical approaches. As a result, current evidence supports the biological plausibility and potential clinical relevance of circulating microRNAs but does not yet justify their routine use for prognostic stratification in pediatric practice.

Future research should prioritize large, multicenter pediatric cohorts, standardized specimen handling and analytical pipelines, transparent reporting of hazard ratios with confidence intervals, and independent validation of candidate microRNA biomarkers. With improved methodological rigor and reproducibility, circulating microRNAs may ultimately contribute to refined risk stratification and minimally invasive prognostic monitoring in pediatric hematologic malignancies.

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