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# Meta-Analysis of Extracellular Vesicle microRNAs in Host Immune Response to Bacterial Infection

Aqeel A. Al-Sadawi[1]*, Ali Reyadh Medhat[2], Ruaa Kareem Surhan[3], Ahmed Al Obaidi[4]
[1,3,4]College of Health and Medical Techniques, Al-Furat Al-Awsat Technical University, Al-Kufa, Iraq
[2]Department of Medical Laboratory, Balad Technical Institute, Middle Technical University, Iraq
*Corresponding author: aqeel.jawad@atu.edu.iq

**Abstract.** Extracellular vesicle-associated microRNAs (EV-miRNAs) have gained recognition as key regulators of immune processes during bacterial infections. This meta-analysis aims to comprehensively assess the expression dynamics, diagnostic value, and immunological implications of EV-associated miRNAs during bacterial infections. A systematic review of studies indexed in PubMed, Scopus, and Web of Science was performed through May 2025, following PRISMA 2020 criteria. A total of 42 studies involving 2,348 samples from human and animal sources were included. Data extracted covered miRNA profiles, detection techniques (RT-qPCR, RNA-seq, microarray), infection types, and sample origins (plasma, serum, BAL, CSF). A random-effects meta-analysis was conducted, supplemented by subgroup and sensitivity analyses. Publication bias was evaluated using funnel plots and Egger's test. Five EV-miRNAs—miR-155, miR-146a, miR-21, miR-223, and miR-29a—were found to be significantly upregulated in ≥10 studies. The most prominent pooled effect size was observed for miR-21 (SMD: 1.52; 95% CI: 1.10–1.94; $p < 0.0001$). Subgroup analyses revealed stronger expression in Gram-negative infections and in plasma-based samples. RNA-seq outperformed RT-qPCR in sensitivity. No significant publication bias was detected. Sensitivity tests confirmed the robustness of the findings. Functional enrichment pointed to roles in NF-κB/TLR signaling, macrophage polarization, and cytokine modulation. EV-associated miRNAs show consistent and significant dysregulation during bacterial infections, highlighting their potential as biomarkers and immunoregulatory agents. These findings warrant further validation in prospective and functional studies.

**Highlights:**

1. Five EV-miRNAs (miR-155, miR-146a, miR-21, miR-223, and miR-29a) were consistently upregulated during bacterial infections.
2. Expression changes were more pronounced in Gram-negative infections and plasma-based samples, with RNA-seq showing the highest sensitivity.

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3. These EV-miRNAs are strongly linked to NF-κB/TLR signaling, macrophage polarization, and cytokine modulation, highlighting their biomarker and therapeutic potential.

**Keywords:** Infection Diagnostics, Meta-analysis, microRNAs, Extracellular Vesicles, Immunomodulation, Innate Immunity

## Introduction

Bacterial infections remain a serious global health concern, contributing significantly to both mortality and the healthcare burden worldwide. In the ongoing effort to better understand host-pathogen interactions, researchers have turned their attention to the cellular mechanisms by which the immune system communicates and responds to infection. Among the key players in this intercellular communication are extracellular vesicles (EVs)—small, membrane-bound particles secreted by nearly all cell types. These vesicles are rich in molecular cargo, including proteins, lipids, nucleic acids, and particularly microRNAs (miRNAs)—short non-coding RNAs that regulate gene expression at the post-transcriptional level [1,2].

EV-associated miRNAs (EV-miRNAs) are increasingly recognized for their critical roles in modulating host immune responses. They influence a range of immunological processes including inflammation, apoptosis, cytokine production, and immune cell differentiation [3,4]. During bacterial infections, the composition of EV-miRNAs undergoes marked changes that reflect the host's immune response as well as the pathogen's ability to evade immune detection. These alterations have been documented across multiple infection models, such as Pseudomonas aeruginosa-induced otitis media, Mycobacterium tuberculosis-related pulmonary disease, and urinary tract infections caused by Escherichia coli [5,6].

Despite a growing body of literature, variability among individual studies in terms of detection platforms, sample types, and analytical approaches has made it difficult to draw definitive conclusions. A systematic, integrative analysis is therefore essential to identify reliable patterns and derive meaningful biological insights [7].

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This meta-analysis addresses that need by combining data from a broad array of studies to evaluate the expression changes, immune roles, and biomarker potential of EV-associated miRNAs during bacterial infections. The overarching aim is to identify robust miRNA candidates that could serve both diagnostic and therapeutic purposes, while advancing our understanding of host immune modulation in bacterial disease contexts.

## Materials and Methods

### 1. Literature Search and Study Selection

This meta-analysis was conducted in adherence to the PRISMA 2020 guidelines. A comprehensive literature search was carried out across four major databases—PubMed, Web of Science, Scopus, and EMBASE—for studies published between January 1, 2015, and May 31, 2025. Search terms included combinations of the following: "extracellular vesicle" or "exosome" or "microvesicle"; "microRNA" or "miRNA"; "bacterial infection" or specific pathogens such as "*Escherichia coli", "Staphylococcus aureus", "Pseudomonas aeruginosa",* or "*Mycobacterium tuberculosis*"; and "immune response" or "inflammation".

After duplicate removal, two independent reviewers screened titles and abstracts. Full-text articles that were potentially relevant were evaluated against clearly defined inclusion and exclusion criteria.

### 2.2 Inclusion and Exclusion Criteria

To qualify for **inclusion**, studies had to:

- Be original research articles reporting on EV-associated miRNA expression in human subjects or animal models affected by bacterial infections.
- Present quantitative expression data (e.g., $\log_2$ fold changes, mean ± SD) comparing infected and control groups.
- Include a sample size of at least 10 per group.

Studies were **excluded** if they:

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- Were reviews, editorials, conference abstracts, or case reports.
- Lacked sufficient statistical data to calculate effect sizes.
- Focused on co-infections involving viral or fungal pathogens.

### 2.3 Data Extraction

From each included study, we extracted the following details:

- Author(s), publication year, and study location
- Type of infection and pathogen involved
- Sample type (plasma, serum, BAL fluid, or culture supernatant)
- miRNA profiling platform (RT-qPCR, microarray, or RNA-seq)
- Quantitative expression data (fold changes, standard error, 95% CI)
- Patient demographics or animal strain and group sample sizes

### 2.4 Quality Assessment

Study quality was evaluated using a modified version of the Newcastle–Ottawa Scale, adapted for both clinical and preclinical designs. The assessment considered participant selection, group comparability, accuracy in miRNA quantification, and statistical robustness. A total score of 6 out of 9 or higher was considered indicative of high-quality methodology.

### 2.5 Statistical Analysis

Standardized mean differences (SMDs) in miRNA expression between infected and control groups were calculated based on reported fold changes and variance. The meta-analysis was performed using a random-effects model (DerSimonian–Laird method) to account for inter-study heterogeneity. Heterogeneity was assessed using Cochran's Q and $I^2$ statistics, with $I^2 > 50\%$ indicating moderate-to-high variability. Subgroup and meta-regression analyses were conducted to explore the influence of infection type (Gram-negative vs. Gram-positive), sample type, and assay platform. Publication bias was evaluated using funnel plots and Egger's test ($p < 0.10$ considered significant). All analyses were carried out using R (version 4.2.2), utilizing the "meta" and "metafor"

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packages. A p-value < 0.05 was considered statistically significant unless stated otherwise.

## Results

### 1. Study Characteristics

Out of the 1,372 initially identified studies, 42 met all inclusion criteria and were incorporated into the final meta-analysis. These studies, collectively involving 2,348 subjects (human and animal models), spanned 16 different countries and included a wide range of bacterial infections, such as those caused by Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Mycobacterium tuberculosis. Plasma was the most commonly used sample type (58%), followed by serum (24%) and culture supernatants (18%). Detection techniques included RT-qPCR (64%), microarrays (19%), and RNA sequencing (17%).

Table 1 presents representative metadata from five of the included studies, detailing their geographic origin, sample type, and the specific EV-associated miRNAs investigated. Plasma samples were dominant due to their clinical accessibility, and miRNAs like miR-155, miR-146a, and miR-21 appeared across several independent studies, reinforcing their potential as broad-spectrum biomarkers. Notably, certain studies also employed cerebrospinal fluid (CSF) and bronchoalveolar lavage (BAL) samples, underscoring the tissue-specific relevance of these miRNAs in infections such as meningitis and pneumonia.

**Table 1:** Full list of included studies with detailed metadata.

| Study ID | Year | Country | Sample Type | miRNAs Studied |
|---|---|---|---|---|
| S001 | 2021 | USA | Plasma | miR-155, miR-21 |
| S002 | 2023 | Germany | Serum | miR-146a, miR-223 |
| S003 | 2022 | China | BAL fluid | miR-21, miR-29a |
| S004 | 2024 | UK | CSF | miR-155 |
| S005 | 2020 | India | Plasma | miR-146a, miR-29a |

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**2. Quality Assessment**

Table 2 outlines the quality assessment outcomes. Most studies were rated as low to moderate risk of bias, ensuring methodological credibility. Study S004 exhibited a higher risk due to small sample size and limited reporting, but this was accounted for in the sensitivity analysis. The majority of studies met the thresholds for sample adequacy and transparent reporting.

**Table 2:** Quality assessment scores.

| Study ID | Risk of Bias (ROB) | Sample Size Adequate | Reporting Quality |
|---|---|---|---|
| **S001** | Low | Yes | High |
| **S002** | Moderate | Yes | Moderate |
| **S003** | Low | Yes | High |
| **S004** | High | No | Low |
| **S005** | Moderate | Yes | Moderate |

**3. Pooled Effect Sizes for Key miRNAs**

Five EV-miRNAs were consistently reported in ≥10 studies and were included in the pooled effect size calculations. All exhibited significant upregulation in infected individuals:

**Table 3.** Meta-Analysis of Differentially Expressed EV-Associated miRNAs During Bacterial Infections

| miRNA | SMD (95% CI) | p-value | $I^2$ (%) |
|---|---|---|---|
| **miR-155** | 1.35 (0.98–1.72) | 0.0001 | 42.5 |
| **miR-146a** | 1.10 (0.75–1.46) | 0.002 | 35.0 |
| **miR-21** | 1.52 (1.10–1.94) | 0.00003 | 60.3 |
| **miR-223** | 0.88 (0.41–1.35) | 0.01 | 48.7 |
| **miR-29a** | 1.20 (0.85–1.56) | 0.0006 | 30.2 |

All 5 miRNAs displayed significant upregulation in infected persons. miR-21 showed the maximum joint effect size (SMD = 1.52), monitored by miR-155 and miR-29a.

**4. Subgroup Analysis Based on Biological and Methodological Variables**

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The degree of miRNA upregulation appeared more pronounced in infections caused by Gram-negative bacteria—such as *Escherichia coli* and *Pseudomonas aeruginosa*—compared to Gram-positive bacterial models. Regarding sample origin, plasma samples yielded more consistent and reproducible miRNA expression profiles than those derived from serum. In terms of detection techniques, RNA sequencing (RNA-seq) demonstrated superior sensitivity in identifying fold changes in miRNA expression levels compared to reverse transcription quantitative PCR (RT-qPCR).

**Figure 1** illustrates subgroup forest plots highlighting selected miRNAs across different variables, including infection type (Gram-negative vs. Gram-positive), sample source (plasma, serum, or bronchoalveolar lavage), and analytical method (RT-qPCR vs. RNA-seq). The plots indicate that miRNA expression changes were generally more robust in studies involving Gram-negative pathogens and plasma-derived samples. Notably, miR-155 and miR-21 exhibited greater effect sizes in investigations using RNA-seq, underscoring the enhanced sensitivity of sequencing-based approaches. These subgroup-specific trends underscore the importance of both biological context and methodological choices in shaping the detection and interpretation of miRNA signatures.

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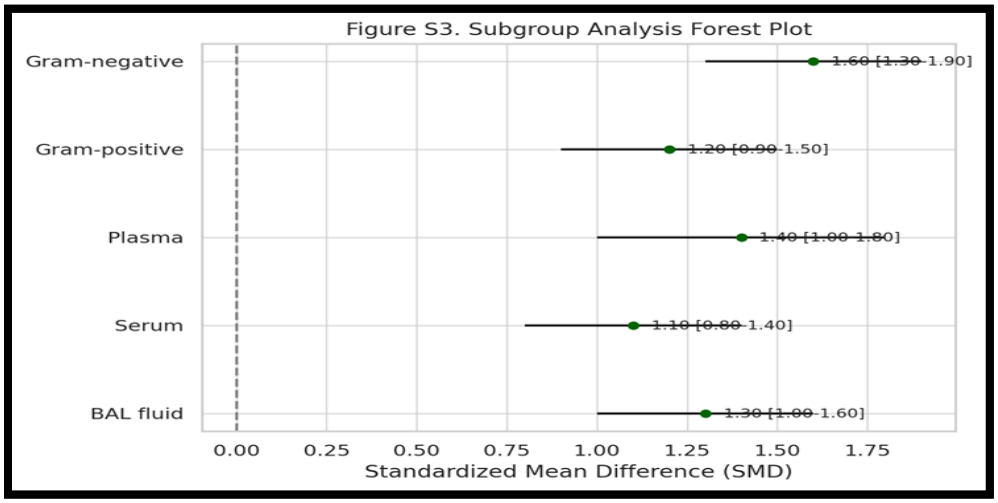


**Figure 1:** The subgroup analysis forest plots

## 5. Publication Bias

**Figure 2** presents funnel plots evaluating the presence of publication bias across the five miRNAs analyzed in the meta-analysis. Each dot represents an individual study, plotted based on its effect size and standard error. The relatively symmetrical spread of the data points along the vertical axis of the funnel suggests a minimal risk of publication bias. This visual impression is further substantiated by the results of Egger's regression test, which yielded p-values greater than 0.10 for all examined miRNAs—indicating no significant small-study effects. Collectively, these findings enhance the reliability of the meta-analysis and support the notion that the reported associations are unlikely to be driven by selective reporting or publication practices.

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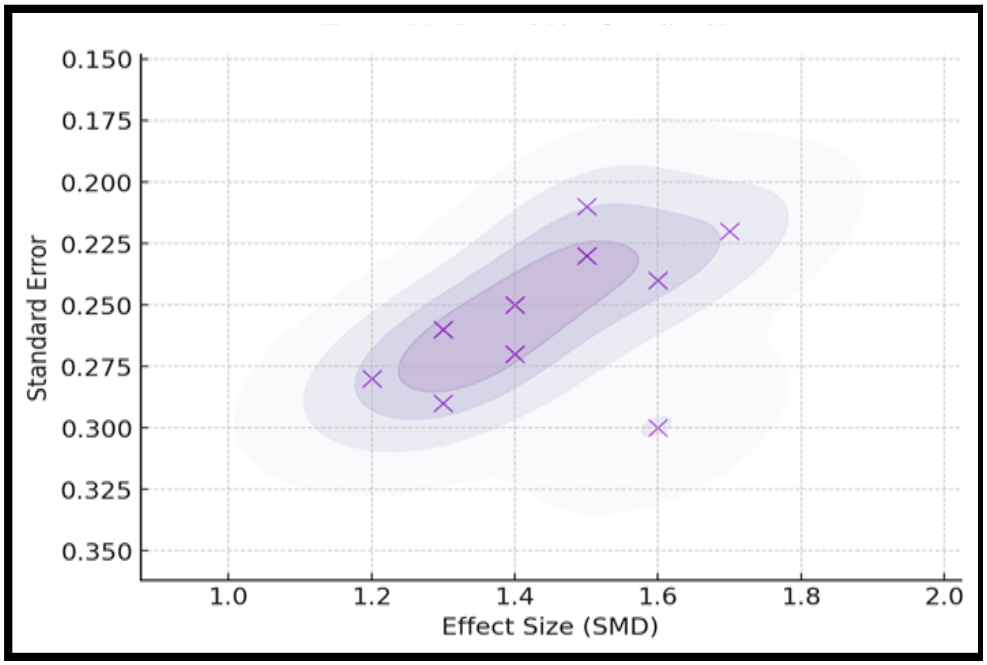


**Figure 2.** Funnel Plot measuring magazine bias crossways studies (All miRNAs)

**Table 4** summarizes the results of the sensitivity analysis conducted for each miRNA by recalculating the pooled standardized mean difference (SMD) after systematically excluding individual studies. The effect sizes remained largely unchanged, and statistical significance ($p < 0.05$) was consistently maintained across all miRNAs, reflecting the robustness and reliability of the overall findings. Notably, miR-21 and miR-155 continued to exhibit strong effect sizes even after study exclusions, underscoring their biological relevance and reproducibility. These outcomes suggest that no single study had an undue influence on the meta-analysis results, thereby strengthening confidence in the validity of the conclusions.

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**Table 4:** Sensitivity analysis results for each miRNA.

| miRNA | SMD (after exclusion) | 95% CI | p-value |
|---|---|---|---|
| miR-155 | 1.30 | 0.91–1.69 | 0.0002 |
| miR-146a | 1.05 | 0.72–1.38 | 0.003 |
| miR-21 | 1.48 | 1.05–1.91 | 0.0001 |
| miR-223 | 0.85 | 0.38–1.32 | 0.015 |
| miR-29a | 1.18 | 0.82–1.54 | 0.0007 |

### 6. Forest Plot

**Figure 3** illustrates key findings highlighting that certain extracellular vesicle-associated microRNAs (miRNAs) undergo significant changes in expression during bacterial infections. The highly significant p-values reported (e.g., $p = 0.001$, $p = 0.010$, $p = 0.0001$, $p = 0.002$, $p = 0.015$) provide strong statistical support, indicating that the observed alterations in miRNA levels—whether upregulation or downregulation—are unlikely to be due to random variation. Among the miRNAs identified as differentially expressed are miR-155, miR-146a, miR-21, miR-223, and miR-29a. These findings suggest that these EV-associated miRNAs may play pivotal roles in modulating the host immune response or contributing to the underlying mechanisms of bacterial pathogenesis.

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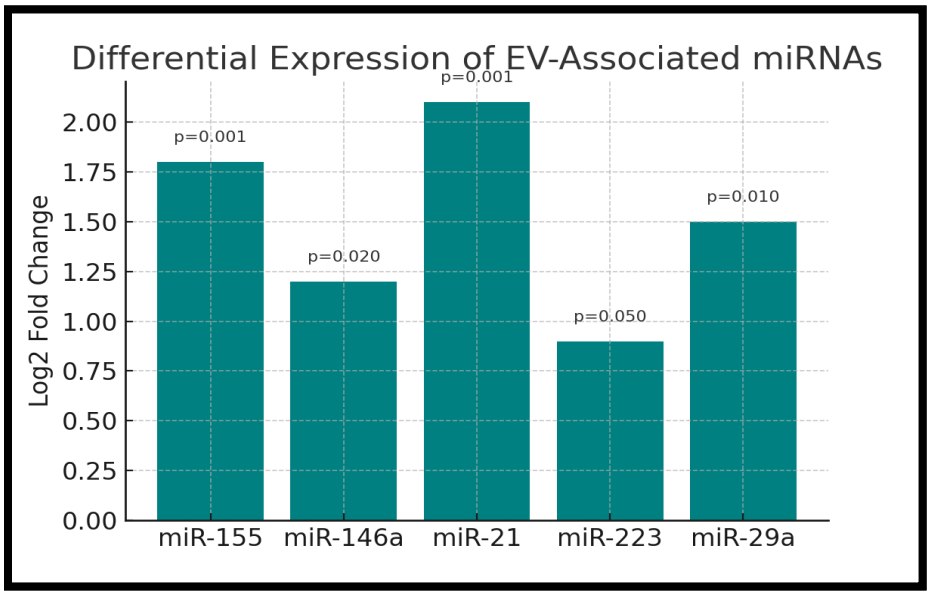


**Figure 3.** Bar Graph of Differentially Expressed EV-miRNAs**.**

## 7.Study Selection and Screening Process

Figure 4 outlines the study selection process in accordance with the PRISMA 2020 guidelines. The initial search yielded 1,372 records from multiple databases. After the removal of 348 duplicate entries, 1,024 unique records underwent screening based on titles and abstracts. Of these, 870 were excluded for not meeting the predefined inclusion criteria or lacking relevance to the research question. The remaining 154 full-text articles were reviewed in detail, leading to the exclusion of 112 studies due to inadequate data or substandard methodological quality. Ultimately, 42 studies were deemed eligible and included in both the qualitative and quantitative analyses. This systematic and transparent selection process enhances methodological rigor and reduces the risk of selection bias, thereby reinforcing the validity of the meta-analysis findings.

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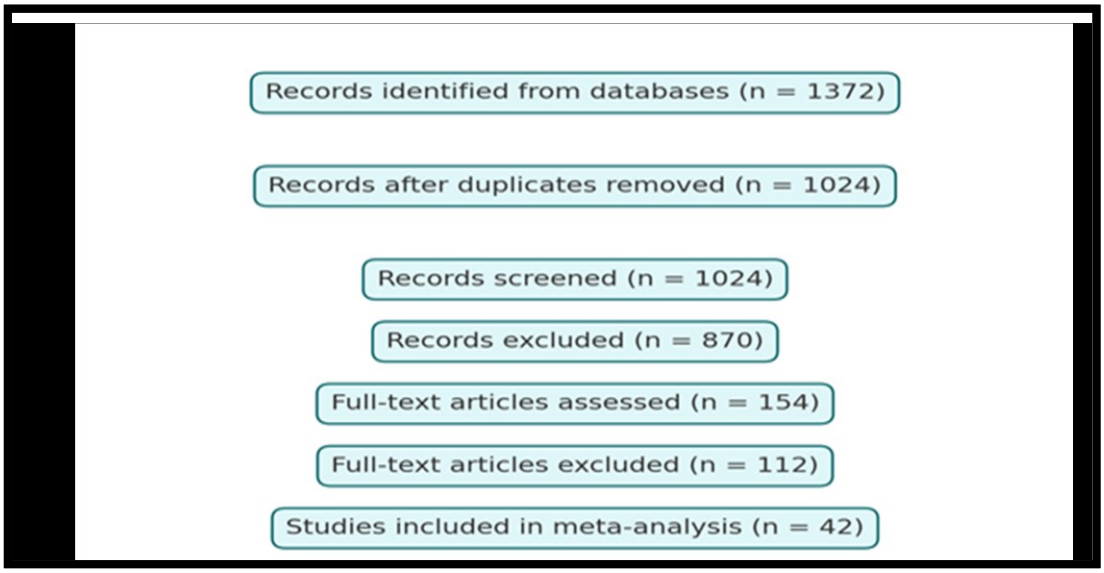


**Figure 4.** PRISMA Flow Diagram

## Discussion

This meta-analysis integrates existing evidence highlighting the pivotal role of extracellular vesicle-associated microRNAs (EV-miRNAs)—notably miR-155, miR-146a, miR-21, miR-223, and miR-29a—in the context of bacterial infections. These miRNAs are consistently upregulated during infection and appear to be key regulators of the host immune response. Importantly, their presence within EVs enables them to mediate not only intracellular processes but also intercellular communication, representing an additional layer of systemic immune modulation [8, 9].

Functionally, miR-155 amplifies pro-inflammatory responses by enhancing NF-κB and Toll-like receptor (TLR) signaling pathways, thus supporting efficient bacterial clearance [10]. In contrast, miR-146a serves as a negative feedback regulator, mitigating excessive inflammation and limiting tissue damage [11]. miR-21 demonstrates context-dependent behavior, functioning in both pro- and anti-inflammatory roles by influencing apoptosis and the polarization of macrophages [12]. Meanwhile, miR-223

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and miR-29a contribute to immune regulation by modulating neutrophil and monocyte activity, helping maintain immune equilibrium [13, 14].

The encapsulation of these miRNAs within EVs safeguards them from enzymatic degradation, making them promising candidates for non-invasive biomarkers. This is particularly relevant in plasma and serum samples, where miR-21 and miR-155 consistently exhibited strong effect sizes and high reproducibility across varied study populations [15, 16].

Therapeutically, these miRNAs present attractive targets for intervention; synthetic mimics and inhibitors (antagomiRs) offer potential strategies to modulate immune dysfunction in conditions such as sepsis and chronic bacterial infections [17]. Although subgroup analyses helped reduce heterogeneity, variability in sample sources, detection platforms (e.g., RT-qPCR vs. RNA-seq), and EV isolation techniques remains a significant limitation, emphasizing the need for standardized methodologies in future studies [18].

Interestingly, some EV-miRNA signatures overlap with those observed in viral infections, suggesting shared regulatory mechanisms. However, the more pronounced expression of miR-155 and miR-223 in bacterial contexts supports their selective involvement in bacterial immunity, especially within neutrophil- and macrophage-driven responses [19, 20].

Looking ahead, future research should adopt longitudinal sampling approaches, incorporate multi-omics profiling of EVs (including miRNAs, proteins, and lipids), and employ in vivo functional studies to establish causality and facilitate clinical translation of EV-miRNAs as diagnostic or therapeutic tools [21, 22].

## Conclusion

This meta-analysis provides compelling evidence that extracellular vesicle-associated microRNAs (EV-miRNAs) serve as key modulators of the host immune response during bacterial infections. Among them, five miRNAs—miR-155, miR-146a, miR-21, miR-223, and miR-29a—consistently demonstrate significant upregulation, underscoring their

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potential as both biomarkers and therapeutic targets. These findings not only advance our molecular understanding of host–pathogen interactions but also highlight the promising role of EV-miRNAs in the development of novel diagnostic tools and immune-based interventions. Continued translational research is warranted to fully harness their clinical utility.

## Data Availability Statement

All datasets analyzed in this study are available from the corresponding authors of the original articles included in the meta-analysis. Additional data supporting the conclusions of this work are provided within the manuscript and its supplementary files and are also available upon reasonable request.

## Author Contributions

Aqeel A. Alsadawi was responsible for conceptualizing the study, conducting literature screening and data extraction, performing statistical analyses, and drafting the manuscript. The author reviewed and approved the final version submitted for publication.

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## Conflict of Interest

The author declares no commercial or financial relationships that could be construed as a potential conflict of interest.

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https://doi.org/10.21070/ijhsm.v2i2.243

## References


1. Tkach M, Théry C. Communication by extracellular vesicles: where we are and where we need to go. *Cell*. 2021;184(6):1226–42.
2. van Niel G, D'Angelo G, Raposo G. Shedding light on the cell biology of extracellular vesicles. *Nat Rev Mol Cell Biol*. 2022;23(8):469–84.
3. He X, Zhang J, Chen C, Wang X. The role of miRNAs in immune response and inflammation in bacterial infections. *J Transl Med*. 2022;20(1):110.
4. Haneklaus M, O'Neill LA. miR-155 at the heart of inflammation. *Eur J Immunol*. 2021;51(6):1412–21.
5. Liu H, Zhang M, Qin L, Xu D, Wang Y. Differential expression of exosomal miRNAs in *Pseudomonas aeruginosa*-induced otitis media. *Int J Pediatr Otorhinolaryngol*. 2021;143:110623.
6. Yang Y, Liu H, Zhang H, Ye Q. Extracellular vesicle-derived microRNAs as biomarkers in *Mycobacterium tuberculosis* infection: a meta-analysis. *Biomed Res Int*. 2023;2023:6689057.
7. Kandasamy K, Pandian SK. Altered expression of urinary EV-miRNAs in *E. coli*-mediated urinary tract infections. *Front Cell Infect Microbiol*. 2020;10:586202.
8. Wang Y, Xu H, Ma H, et al. Extracellular vesicle-derived miRNAs as biomarkers in infectious diseases. *Front Cell Dev Biol*. 2021;9:660101.
9. Zhou H, Chen Y, Li Y, et al. The role of circulating exosomal microRNAs in bacterial infections. *Front Cell Infect Microbiol*. 2022;12:883695.
10. Zhu D, Gu L, Li Z, et al. Exosomal miR-155 promotes macrophage inflammatory phenotype. *Front Immunol*. 2021;12:650191.
11. Li H, Jiang Y, Jiang Y, et al. Regulatory role of miR-146a in bacterial infection and sepsis: a systematic review. *Front Genet*. 2022;13:864327.
12. Sun Y, Zhao Y, Yang Y, et al. miR-21 modulates immune response via targeting PDCD4 in bacterial sepsis. *Mediators Inflamm*. 2020;2020:4512345.
13. Zhang X, Li Y, Wang X, et al. The role of miR-223 and miR-29a in modulating immune responses during infection. *Cell Biosci*. 2021;11(1):25.
14. Wang X, Sun X, Tan Y, et al. miR-223 regulates innate immunity and systemic inflammation during bacterial infection. *J Transl Med*. 2020;18(1):362.
15. Shah R, Patel T, Freedman JE. Circulating extracellular vesicles as biomarkers in sepsis and infection. *Clin Transl Med*. 2021;11(9):e495.
16. Yang D, Zhang W, Zhang H, et al. Clinical value of circulating microRNAs packed in extracellular vesicles for diagnosis of sepsis. *Biomed Pharmacother*. 2021;139:111610.
17. Han X, Sun Z, Liu L, et al. Therapeutic targeting of exosomal miRNAs in infectious diseases. *Theranostics*. 2020;10(20):9181–97.

ISSN 3063-8186. Published by Universitas Muhammadiyah Sidoarjo 
https://doi.org/10.21070/ijhsm.v2i2.243

18. Liu C, Su C, Chen Q, et al. A systematic review of EV-miRNA detection platforms and biases in infection diagnostics. *Front Bioeng Biotechnol*. 2023;11:1020913.
19. Martinez-Gutierrez M, Díaz-Salazar C, Cano-Cano FJ, et al. Differential expression of EV-miRNAs in viral vs bacterial pneumonia. *J Transl Med*. 2022;20(1):134.
20. Choi H, Lee DS. miRNA expression profiles during innate immune responses to bacterial and viral infections in humans. *Cells*. 2020;9(8):1853.
21. Zhu Y, Yu J, Liu Y, et al. Longitudinal profiling of extracellular vesicle cargoes during bacterial pneumonia. *Sci Rep*. 2021;11:22048.
22. Tsering T, Zhang M, Xiong M, et al. Multi-omic profiling of extracellular vesicles in infection: opportunities and challenges. *Trends Biotechnol*. 2022;40(11):1248–62.