ORIGINAL ARTICLE

# Study of MicroRNA-146a Expression and Soluble Triggering Receptor Expressed on Myeloid Cells-1(sTREM-1) Serum Levels in Patients with Sepsis

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## ABSTRACT

***Background****: Sepsis represents a critical condition characterized by organ dysfunction resulting from exaggerated immune response to infection. MiRNA-146a is vital mediators in innate immune and inflammatory responses and its association with pro-inflammatory cytokines production, lipopolysaccharide (LPS)-mediated. TREM-1 is defined as an innate immunity receptor expressed on myeloid cells as monocytes and neutrophils involved in their activation and release of cytokine.* ***Objectives:*** *To study microRNA-146a expression and sTREM-1 serum levels in patients with sepsis compered to control healthy group and assess their diagnostic and prognostic value.* ***Methodology****: This study was carried out on 90 participants: 60 septic patients from ICU Department, Benha University Hospital on the basis of blood culture (positive microbiological culture results) and National Early Warning Score (NEWS), 30 age and sex matched healthy controls. Five ml of venous blood was collected in sterile test tube with no anticoagulants from all participants under complete aseptic condition. Serum was separated and divided in to 2 parts for Real time PCR for measurement miRNA 146-a expression and assess sTREM-1 levels by ELISA.* ***Results:*** *miRNA 146a gene expression increased significantly in the sepsis group compared to the control group ($p<0.001$) with median of $3.05x10^4$. sTREM-1 serum levels were also significantly higher in sepsis patients with a median level of 347.28 ($p<0.001$) against 104.12 in the control group.* ***Conclusion:*** *miRNA-146a and sTREM-1 have excellent diagnostic value in sepsis. They have potential utility in monitoring disease prognosis for better clinical outcomes.*

## INTRODUCTION

Sepsis is defined as a critical condition characterized by organ dysfunction resulting from an abnormal and exaggerated immune response to infection. It is recognized as a major cause of death among hospitalized patients, particularly those in intensive care units (ICU), and poses a worldwide health burden impacting millions annually[1].

Commonly used biomarkers in sepsis diagnosis include procalcitonin (PCT) [2], C-reactive protein (CRP), and interleukin-6 (IL-6). However, their diagnostic utility is often limited by insufficient specificity and sensitivity in differentiating sepsis from other inflammatory conditions.

The problems with these markers are given by their low selectivity and specificity[3].

Microbiological culture still represents the gold standard in distinguishing sepsis from other non-infectious diseases[4]; however, this technique is time-consuming and often related to false negative results. Therefore, it is recommended to investigate novel markers, which can help to identify the sepsis risk timely and monitor prognosis in sepsis patients [5]. Recent studies use new markers for sepsis, such as microRNAs (miRNAs) [6].

MicroRNAs (miRNAs) are short, non-coding RNA sequences—typically 21 to 23 nucleotides in length—present in all body fluids, tissues, and most cell types[7]. Thier function primarily is as post-transcriptional regulators of gene expression [8].

The expression of miRNA-146a in macrophages is known to be stimulated by toll-like receptor activation (notably TLR2, TLR4, and TLR5) [9]. This microRNA plays an immunomodulatory role by suppressing the pro-inflammatory activity of M1-type macrophages and other innate immune cells[10]. Additionally, miRNA-146a downregulates the synthesis of key pro-inflammatory cytokines in macrophages, including TNF-α, IL-1β, and IL-6, thus contributing to a more tolerogenic immune environment. miRNA-146a also exerts its regulatory effects by targeting key signaling intermediates such as

IRAK1 and TRAF6, which in turn modulate the NF-κB and MyD88 pathways involved in innate immune responses.[11].

Triggering receptor expressed on myeloid cells-1 (TREM1) is is a membrane-bound glycoprotein that belongs to the immunoglobulin superfamily. The human TREM-1 is a glycoprotein of size 30- kDa found on the 6p21 chromosome and a type of DNAX activation protein of 12KDa (DAP12) related receptor. It is highly expressed on surface of neutrophils, macrophages, and fully developed monocytes[12].

Upon activation, TREM-1 promotes a robust inflammatory response by stimulating the release of cytokines and chemokines and enhancing upregulation of the gene expression of TREM-1 and surface expression of cell activation markers. This amplification mechanism plays a central role in the pathogenesis of sepsis by exacerbating the dysregulated immune response[13].

**Aim of the study**

Evaluation of miRNA 146a expression and its diagnostic and prognostic value in patients with sepsis.
Measurement of TREM-1 levels in patients with sepsis compared to control group.

## METHODOLOGY

This is a case -control study carried out at Microbiology and Immunology Department and ICU Department, Benha Faculty of Medicine Benha University from April 2023 to May 2025. This study who was carried out on 90 participants, were chosen and classified into: **Sixty** patients suffered from sepsis were selected from ICU Department,Benha University Hospital on the basis of blood culture (positive microbiological culture results) and National Early Warning Score (NEWS). Patients were classified according NEWS score in to : sever (21 patients), moderate (19 patients) and mild (20 patients).

**Thirty** apparently healthy subjects matched for age and sex served as control group.

**Patients were subjected to the followings:** Complete history taking, full clinical examination, laboratory investigations:

**Routine tests:** CBC (complete blood count), C-reactive protein**,** microbiological culture according to infectious source (urine,sputum) in addition to positive blood culture**.**

**Sampling:** Five ml of venous blood was obtained from all participants under complete aseptic condition in free anticoagulant tubes, allowed to clot**.** After centrifugation, serum was separated and divided into 2 parts stored at −80 °C for further investigations:

Real time (quantative) PCR for measurement miRNA 146-a expression**.**

Detection of TREM-1 levels by ELISA

**Real – Time PCR:**

**Isolation of miRNA-146a by TransGen Biotech EasyPure® miRNA Kit (China)**

**cDNA synthesis from miRNA:** Using **TransGen Biotech TransScript® (China)** First-Strand cDNA Synthesis SuperMix. According manufacturer's instructions. The reverse transcription program was run by using a thermo cycler as following: reverse transcription at 42°C for 10 minutes then inactivation 85°C for 5 seconds.

**measurement of miRNA 146a expression in sample by using TransGen Biotech PerfectStart Green qPCR SuperMix (China) using miRNA 146a primer sequences[14]:**

| | |
|---|---|
| **miRNA146a forward sequence** | 5′-GAACTGAATTCCATGGGTTGTGT-3′ |
| **miRNA146a reverse sequence** | 5′-GCCCACGATGACAGAGAGATCC-3′ |

Amplification was done on a Rotor-Gene Q realtime PCR machine (Qiagen; Germany) using the following PCR thermal cycle conditions: It started with an initial heat activation step at 94°C for 30 seconds for activation of HotStar Taq DNA polymerase. Followed by 40-45 cycles of denaturation at 94°C for 5 seconds, annealing and extension at 60°C at 30 seconds.Relative expression level of miRNA146a was evaluated by the 2^−delta cycle threshold (2 ^ -ΔΔCT) method as shown in figure (1) and (2)

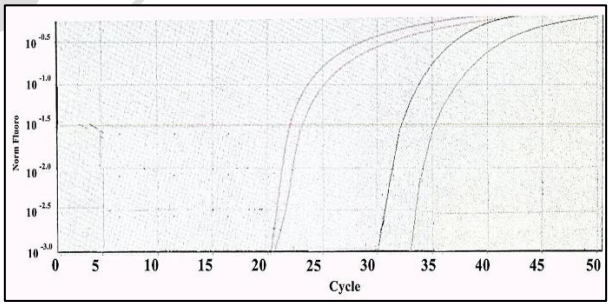


**Fig. 1:** Amplification curves of housekeeping gene expression and miRNA-146a expression in control group

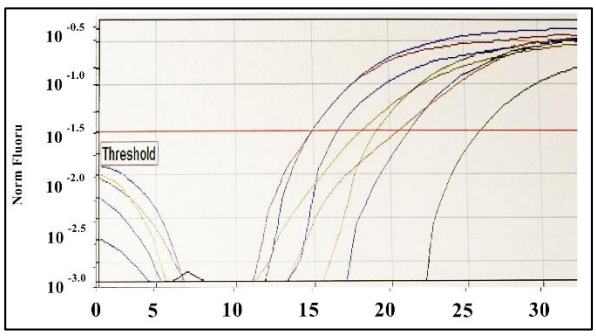


**Fig. 2**: Amplification curves of housekeeping gene expression and miRNA-146a expression in sepsis group.

**Detection of Human sTREM-1 (soluble Triggering Receptor Expressed on Myeloid Cells-1) by Elabscience®ELISA Kit**: The quantification of Human soluble Triggering Receptor Expressed on Myeloid Cells-1 (sTREM-1) was performed using the Elabscience® Sandwich ELISA kit. In this method, the wells of the provided microplate were pre-coated with a capture Human sTREM-1 antibody. The enzymatic reaction was stopped by adding a stop solution, which turned the color to yellow. Absorbance was measured at 450 ± 2 nm using a microplate reader. The optical density (OD) values were directly proportional to the concentration of sTREM-1 in the samples, and sample concentrations were calculated by referencing the standard curve illustrated in Figure (3).

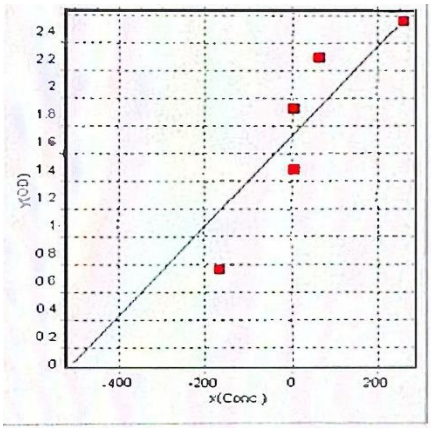


**Fig. 3:** Standard curve of human sTREM-1 ELISA showing the linear relationship between concentration and optical density (OD)

## RESULTS

*Klebsiella pneumoniae* was found to be the most common bacterial cause of sepsis in patients (40%), followed by *Acinetobacter baumannii* (16.7%) as shown in table (1)

**Table 1: Isolated causative organisms among sepsis patients.**

| | Sepsis n = 60 | |
|---|---|---|
| | № | % |
| **Causative organisms** | | |
| Klebsiella pneumonia | 24 | 40.0 |
| Acinetobacter baumannii | 10 | 16.7 |
| Proteus mirabilis | 9 | 15.0 |
| Pseudomonas eurogenosum | 10 | 16.7 |
| Staphylococcus aureus | 2 | 3.3 |
| MRSA | 1 | 1.7 |
| CoNS | 3 | 5.0 |
| Staphylococcus epidermidis | 1 | 1.7 |
| Staphylococcus hominis | 3 | 5.0 |

№, number.

MiRNA 146a gene expression increases significantly in the sepsis group as compared to the control group ($p<0.001$). The miRNA-146a gene expression showed up regulation in sepsis group, with median of $3.05x10^4$ as shown in table (2).

sTREM-1 levels in the sepsis and control groups reveals a considerable increase in the sepsis group, with a median level of 347.28 against 104.12 in the control group ($p<0.001$) as shown in table (3).

**Table 2: miRNA-146a gene expression in sepsis and control groups.**

| | Sepsis n = 60 | Control n = 30 | Test | P |
|---|---|---|---|---|
| **miRNA-146a gene expression** | | | | |
| Mean ± SD. | $1.06x10^5 \pm 2.45x10^5$ | 1.0 ± 0.0 | U= 0.0* | <0.001* |
| SE. | $3.17x10^4$ | 0.0 | | |
| Median | $3.05x10^4$ | 1.0 | | |
| Min. – Max. | $1.48x10^3 – 1.70x10^6$ | 1.0 – 1.0 | | |

SD. Standard deviation, SE. Standard error, Min.: Minimum, Max.: Maximum, U: Mann–Whitney test, p: Comparing sepsis and control, *: Significant when p value <0.05.

**Table 3: sTREM-1 levels in sepsis and control groups.**

| | Sepsis n = 60 | Control n = 30 | Test | P |
|---|---|---|---|---|
| **sTREM-1 (pg/mL)** | | | | |
| Mean ± SD. | 348.43 ± 66.02 | 128.79 ± 35.62 | U= 1.0* | <0.001* |
| Median | 347.28 | 104.12 | | |
| Min. – Max. | 275.62 – 497.04 | 103.00 – 192.82 | | |

SD. Standard deviation, SE. Standard error, Min.: Minimum, Max.: Maximum, U: Mann–Whitney test, p: Comparing sepsis and control, *: Significant when p value <0.05.

MiRNA-146a gene expression levels and the severity of sepsis varies significantly among spesis groups. Patients with severe sepsis had much greater levels of miRNA 146a than those with mild or moderate sepsis (medians= $1.29\times10^5$, $1.32\times10^4$ and $5.78\times10^3$ respectively) as shown in table (4)

sTREM-1 levels and the degree of sepsis varies significantly between severity groups. Severe sepsis patients have the greatest sTREM-1 levels, followed by those with moderate to mild sepsis. The statistical analysis shows a substantial association between rising severity of sepsis and elevated sTREM-1 levels as shown in table (5)

The findings show that both miRNA-146a gene expression and sTREM-1 levels are significantly effective at distinguishing sepsis patients from the control group. The miRNA 146a has an area under the ROC curve (AUC) of 1.0, suggesting perfect discrimination with 100% sensitivity and specificity. Similarly, sTREM-1 has an AUC of 0.999, sensitivity of 98.3%, and specificity of 96.67% as shown in table (6) and figure (4).

**Table 4: Association between miRNA-146a gene expression and degree of sepsis among sepsis patients.**

| | miRNA-146a gene expression | | | | Test | P |
|---|---|---|---|---|---|---|
| | Mean ± SD. | SE. | Median | Min. – Max. | | |
| **Degree of sepsis** | | | | | | |
| Mild, n=20 | $2.04\times10^4 \pm 3.25\times10^4$ | $7.26\times10^3$ | $5.78\times10^3$ | $1.48\times10^3 – 1.44\times10^5$ | H= 36.764* | <0.001* |
| Moderate, n=19 | $2.64\times10^4 \pm 2.85\times10^4$ | $6.53\times10^3$ | $1.32\times10^4$ | $1.48\times10^3 – 1.07\times10^5$ | | |
| Severe, n=21 | $2.59\times10^5 \pm 3.71\times10^5$ | $8.10\times10^4$ | $1.29\times10^5$ | $6.82\times10^4 – 1.70\times10^6$ | | |

Median with small different letters are significant, SD. Standard deviation, SE: Standard error, Min.: Minimum, Max.: Maximum, H: Kruskal-Wallis test, *: Significant when p value <0.05.

**Table 5: Association between sTREM-1 level and degree of sepsis among sepsis patients.**

| | sTREM-1 level | | | | Test | P |
|---|---|---|---|---|---|---|
| | Mean ± SD. | SE. | Median | Min. – Max. | | |
| **Degree of sepsis** | | | | | | |
| Mild, n=20 | 295.75 ± 35.62 | 8.38 | 279.39 | 275.62 – 390.42 | H= 43.784* | <0.001* |
| Moderate, n=19 | 327.96 ± 43.89 | 10.07 | 277.41 | 277.41 – 395.01 | | |
| Severe, n=21 | 417.14 ± 40.77 | 8.90 | 300.47 | 300.47 – 497.04 | | |

Median with small different letters are significant, SD. Standard deviation, SE: Standard error, Min.: Minimum, Max.: Maximum, H: Kruskal-Wallis test, *: Significant when p value <0.05.

**Table 6 : Validity of miRNA-146a gene expression and sTREM-1 for discrimination between sepsis and the control group.**

| AUC | 95 CI | P | Cut off | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|---|---|
| **miRNA-146a gene expression** | | | | | | | | |
| 1.0 | 1.0-1.0 | <0.001* | >1 | 100 | 100 | 100 | 100 | 100 |
| **sTREM-1 level** | | | | | | | | |
| 0.999 | 0.998-1.0 | <0.001* | >275.62 | 98.3 | 96.67 | 98.4 | 96.8 | 98.9 |

AUC: Area under ROC curve; CI: Confidence interval, PPV, positive predictive value; NPV, negative predictive value. *: P value Significant <0.05.

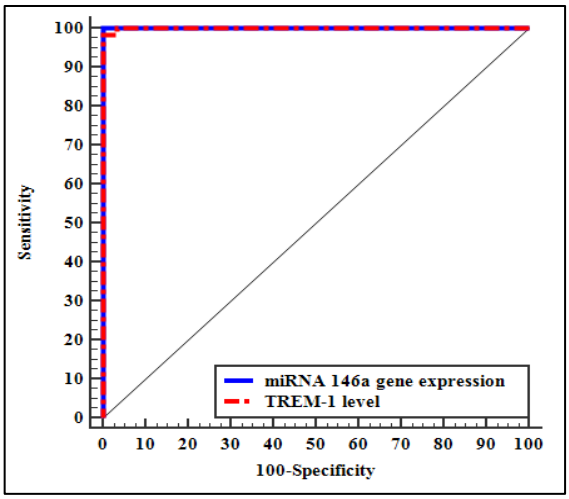


**Fig. 4:** ROC Curve for miRNA-146a gene expression and sTREM-1

## DISCUSSION

This study showed no significant difference in gender (p= 0.881) and age (p= 0.385) distribution between the sepsis group and control group.

This study showed that *klebsiella pneumoniae* was the predominant pathogen in sepsis cases (40%), followed by *Acinetobacter baumannii* and *Pseudomonas spp.* (each ~16.7%). This correlates with Cristina et al[15] who stated that *K. pneumoniae* as one of the most common causes of nosocomial Gram-negative bacteraemia and pneumonia, especially in intensive care settings

This result also was in agreement with a finding from *multicenter Indian registry*[16] which reported that Gram-negative infections—especially *Escherichia coli, Klebsiella spp. and Acinetobacter spp.*—were responsible for the majority of sepsis cases, with a high rate of carbapenem resistance and the highest mortality rates observed among these infections.

This study also showed that, miRNA-146a expression was significantly upregulated in the sepsis group (median = $3.05 \times 10^4$, $p < 0.001$), which agrees with recent meta-analytic evidence confirming its prognostic utility. *Jin et al* [17] identified miR-146a among several miRNAs demonstrating high predictive value for sepsis-related mortality (SROC up to 0.84) and stated that peripheral blood miR-146a levels in the sepsis group elevated in comparison with the control group.

Additionally, Chen et al[8] has reported that miR-146a levels are significantly elevated in the serum of septic patients compared to healthy controls. The expression correlates with disease severity, organ dysfunction scores, and prognosis, suggesting its possible role as marker for both diagnosis and prognosis.

Another study also revealed that in septic patients, plasma miR-146a concentrations are elevated and closely associated with sepsis out comes[18].

In our study, there was a significant elevation in sTREM-1 levels among sepsis patients compared to the control group (median: 1.702 vs. 0.094; $p < 0.001$). This finding was supported with previous studies that demonstrated a pronounced increase in sTREM-1 expression in sepsis [19], which reported median sTREM-1 levels of 850 pg/mL in infected pediatric ICU patients compared to 67.5 pg/mL in healthy controls, with a statistically significant difference ($p < 0.001$).

This is in agreement with *A multicenter prospective study published in 2025* confirmed the diagnostic and prognostic importance of sTREM-1 in sepsis. It demonstrated that sTREM-1 was significantly increased in septic patients and had strong discriminative power for sepsis diagnosis and severity assessment [20].

Similarly, Theobald et al [21] found that sTREM-1 is more accurate than any other clinical or laboratory findings to expect the presence of bacterial or fungal infections. sTREM-1 might also be useful as a marker of disease severity in different inflammatory settings, especially when an inadequate immune response results in a fatal outcome. Patients with septic shock show extremely high sTREM-1 levels compared with healthy controls (814 pg/mL compared with 1.77–135 pg/mL).

The results also showed a marked increase in miRNA-146a expression with the progression of sepsis severity, with medians of $5.78 \times 10^3$, $1.32 \times 10^4$, and $1.29 \times 10^5$ for mild, moderate, and severe cases, respectively. This graded elevation is consistent with findings by *Wang et al* [22], who reported that miRNA-146a levels were significantly higher in severe sepsis compared to non-severe cases, suggesting its association with disease progression. *Li et al* [23] further confirmed that miRNA-146a is consistently upregulated in septic patients with poor outcomes, and highlighted its prognostic significance in assessing sepsis severity and mortality.

The study result analysis revealed that sTREM-1 levels increased progressively with sepsis severity, being highest in severe cases, intermediate in moderate, and lowest in mild sepsis. This dose–response pattern corroborates findings by Jiang et al[24] who reported that serum sTREM-1 levels were significantly increased in severe and shock-phase sepsis groups than in mild cases, reflecting its potential utility in monitoring disease progression.

In our study, both miRNA-146a gene expression and sTREM-1 levels demonstrated excellent diagnostic performance in distinguishing sepsis patients from the control group. The ROC curve analysis revealed that miRNA-146a achieved an AUC of 1.0, with 100% sensitivity and 100% specificity, indicating perfect discrimination between septic and non-septic

individuals. This finding is consistent with the results reported by *Nour et al* [25], who showed that miRNA-146a had AUC = 1.00, sensitivity = 100%, and specificity = 100% in pediatric sepsis patients, suggesting its strong potential as a diagnostic marker for sepsis.

In this study, sTREM-1 exhibited excellent diagnostic performance in differentiating sepsis patients from the control group, with an area under the ROC curve (AUC) of 0.999, 100% sensitivity, and 96.67% specificity. These values suggest that sTREM-1 may serve as a highly effective marker for the diagnosis of sepsis.

This finding is supported by a study conducted by Guo et al[26], which investigated the diagnostic value of serum sTREM-1 in patients with spontaneous bacterial peritonitis. The study reported an AUC of 0.981 (95% CI: 0.962–0.999), with 93.3% sensitivity and 95.5% specificity, highlighting the strong discriminative ability of sTREM-1 in identifying bacterial infections associated with systemic inflammatory responses.

## CONCLUSION

This study shows that miRNA-146a expression and sTREM-1 levels were significantly higher in patients with sepsis compared to controls, with strong correlations to inflammatory markers and sepsis severity. They could act as reliable diagnostic tools for early recognition of sepsis and their potential use in monitoring disease prognosis for better clinical outcomes. Their relationship with severity of sepsis supports their possible use as therapeutic targets in treatment.

**Declarations:**

**Consent for publication**: Not applicable

**Availability of data and material:** Data are available upon request.

**Competing interests:** The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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## REFERENCES

1. Braun D. A retrospective review of the sepsis definition after publication of sepsis-3. Am J Med; 132:382–4
2. Sinha M, Desai S, Mantri S, Kulkarni A. Procalcitonin as an adjunctive biomarker in sepsis. Indian Journal of Anaesthesia. 2011; 55(3):266-70.
3. Trancă SD, Petrişor CL, Hagău N. Biomarkers in polytrauma induced systemic inflammatory response syndrome and sepsis - a narrative review. Rom J Anaesth Intensive Care. 2014; 21(2):118-22.
4. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H and Opal SM. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock. Crit Care Med. 2012; 41(2):580-637
5. Saswati Banerjee1, Winston E. Thompson1, Indrajit Chowdhury. Emerging roles of microRNAs in the regulation of Toll-like receptor (TLR)-signaling, Frontiers in Bioscience, Landmark. 2021; 26:771-796
6. Acuña SM, Floeter-Winter LM, Muxel SM. MicroRNAs. Biological Regulators in PathogenHost Interactions. 2020; Cells, 9 (1), 113.
7. O'Connell RM, Rao DS, Chaudhuri AA, Baltimore D. Physiological and pathological roles for microRNAs in the immune system. Nat. Rev. Immunol. 2010; 10: 111–122
8. Chen L, Yu L, Zhang R, Zhu L, Shen W. Correlation of microRNA-146a/b with disease risk, biochemical indices, inflammatory cytokines, overall disease severity, and prognosis of sepsis. Medicine (Baltimore). 2020; May 29;99(22):e19754.
9. Halushka MK, Fromm B, Peterson KJ, McCall MN. Big strides in cellular microRNA expression. Trends Genet. 2018; 34:165–167.
10. Juzenas S, Venkatesh G, Hubenthal M, Hoeppner MP, Du ZG, Paulsen M. A comprehensive, cell specific microRNA catalogue of human peripheral blood. Nucleic Acids Res. 2017; 45:9290–9301.
11. Barbu MG, Condrat CE, Thompson DC, Bugnar OL, Cretoiu D. Toader, O.D. et al. MicroRNA involvement in signaling pathways during viral infection. Front. Cell Dev. Biol.2020; 8:143.
12. Pelham CJ, Pandya AN, Agrawal DK. Triggering receptor expressed on myeloid cells receptor family modulators: a patent review. Expert Opin Ther Pat. 2014; 24:1383–1395.
13. Dantas PHDS, Matos AO, da Silva Filho E, Silva-Sales M and Sales-Campos H. Triggering Receptor Expressed on Myeloid Cells-1 (TREM-1) as a Therapeutic Target in Infectious and Noninfectious Disease: A Critical Review. Int Rev Immunol. 2020; 39(4):188–202.
14. Zhao Q, Wang Y, Zou J, Kuang R, Ji S. MiR-146a alleviates acute lung injury via inhibiting Notch 1 signaling pathway targeting macrophage. Cell Mol Biol (Noisy-le-grand. 2024 Jan 31;70(1):34-39.
15. Cristina ML, Alicino C, Sartini M, Faccio V, Spagnolo AM, Bono VD et al. Klebsiella

pneumoniae research group. Epidemiology, management, and outcome of carbapenem-resistant Klebsiella pneumoniae bloodstream infections in hospitals within the same endemic metropolitan area. J Infect Public Health. 2018 Mar-Apr;11; (2):171-177. Epub 2017 Jun 28. PMID: 28668656

16. Todi S, Mehta Y, Zirpe K, Dixit S, Kulkarni AP. Gurav S.*et al.* A multicentre prospective registry of one thousand sepsis patients admitted in Indian ICUs. (SEPSIS INDIA) study. Crit Care. 2014; 28, 375.
17. Jin YX, Zhang Y, Li YF, Zheng XL. Significances of miRNAs for predicting sepsis mortality: a meta-analysis (2025). Frontiers in Microbiology. https://doi.org/10.3389/fmicb.2025.1472124
18. Wang S, Yang Y, Suen A, Zhu J, Williams B, Hu J, Chen F, et al. Role of extracellular microRNA-146a-5p in host innate immunity and bacterial sepsis (2021). iScience. 24(12):103441.
19. Özsoy HG, Ataman M, Şahin SK, Şenocak İ, Varlibaş A, Yuvanç E. et al. Diagnostic utility of soluble TREM-1 in pediatric sepsis in intensive care settings (2024). Pediatric Critical Care Medicine, 25(3), 145–152.
20. Smith AJ, Martinez LE, Zhao W. Diagnostic and predictive values of soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) in sepsis: A multicenter prospective cohort. Critical Care Medicine. 2025; 53(1):112–120.
21. Theobald V, Schmitt FCF, Middel CS, Gaissmaier L, Brenner T, Weigand MA. Triggering receptor expressed on myeloid cells-1 in sepsis, and current insights into clinical studies. Crit Care. 2024 Jan 9;28(1):17.
22. Wang Y, Zhang J, Liu X. Diagnostic and prognostic value of circulating microRNAs in sepsis: A meta-analysis. Frontiers in Immunology. 2023; 14, 1134567. https://doi.org/10.3389/fimmu.2023.1134567
23. Li H, Sun R, Zhao Q. MicroRNA-146a as a prognostic biomarker in sepsis: Evidence from integrated transcriptomic analysis and clinical validation. Frontiers in Microbiology. 2025; 16, Article 1287654. https://doi.org/10.3389/fmicb.2025.1287654
24. Jiang S, Liu L, Zhu X. Correlation of serum H-FABP, sTREM-1, and HMGB1 levels with severity and prognosis of sepsis. American Journal of Translational Research. 2024; 16(10):5846–5855. https://doi.org/10.62347/KELZ4296
25. Nour ZA. El-Hamamsy K, Ehsan I, Fawaz L, Shaker O, Mossallam D, ElGindy H. MicroRNAs as Potential Diagnostic New Biomarkers in Diagnosis of Sepsis in Pediatric Patients. Rep Biochem Mol Biol. 2022; 11 (2):327-335.
26. Guo, Qiang, Xu, Chuanqin, Sun, Chao, Zhao, Yubao and Zhang, Weifu. "Soluble myeloid triggering receptor expressed on myeloid cell 1 might have more diagnostic value for bacterial ascites than C-reactive protein". Open Life Sciences. 2018; 13(1):456-462.