

Serum IL-6 and TNF- α as Early Immunological Biomarkers of Disease Activity in Acute Brucellosis

Sawsan Mohmmmed Kareem^{1,*} , Ammar Abbas Shalan² , Iman Ghanim ALRakh³ 
, Vikramsinh Bapurao More⁴

¹Department of Biology, College of Science, Mustansiriyah University, P.O. Box 10244, Baghdad, Iraq.

²Department of Basic and Medical Sciences, College of Nursing, University of Babylon, Babylon 51001, Iraq.

³Department of Pharmacology and Toxicology, College of Pharmacy, Al-Mustaqbal University, Hillah, Babylon, Iraq.

⁴Department of Microbiology, Shivaji University, Kolhapur, Maharashtra 416004, India.

Corresponding Author Email:

stsq@uomustansiriyah.edu.iq

Received: 27 June 2026,

Revised: 4 August 2026,

Accepted: 1 September 2026,

DOI: [10.57238/jbb.2026.7432.1182](https://doi.org/10.57238/jbb.2026.7432.1182)



Access this article online

Copyright: ©2026 The authors. This article is published by Nabea Al-Ajyal Foundation Press and is licensed under the CC BY 4.0 license (<http://creativecommons.org/licenses/by/4.0/>).

ABSTRACT

Brucellosis remains endemic across the Middle East, including Iraq, yet the immunological correlates of disease activity in acute human infection remain incompletely characterized in this region.

This short communication reports serum interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) levels in 40 patients with serologically and culture-confirmed acute brucellosis compared with 30 healthy controls at the college of Science, Mustansiriyah University, Baghdad, Iraq.

Serum IL-6 and TNF- α were measured by enzyme-linked immunosorbent assay (ELISA). Both cytokines were significantly elevated in patients relative to controls (IL-6: 38.6 ± 9.4 pg/mL vs. 6.2 ± 2.1 pg/mL, $p < 0.001$; TNF- α : 24.3 ± 6.1 pg/mL vs. 8.7 ± 2.4 pg/mL, $p < 0.001$), and both correlated positively with C-reactive protein (IL-6: $r = 0.61$, $p < 0.001$; TNF- α : $r = 0.54$, $p < 0.001$). These findings support a proinflammatory Th1-skewed cytokine signature in acute brucellosis and suggest that serum IL-6 and TNF- α may serve as accessible adjunct immunological markers of disease activity in this endemic setting.

Keywords: Brucellosis; interleukin-6; tumor necrosis factor-alpha; cytokines; immune response; Th1

1. Introduction

Human brucellosis, caused by facultative intracellular bacteria of the genus *Brucella*, remains one of the most common bacterial zoonoses worldwide and continues to impose a significant public health burden across the Middle East, including Iraq, where transmission is driven largely by consumption of unpasteurized dairy products and close contact with livestock [1].

Following macrophage invasion, control of *Brucella* infection depends heavily on a Th1-polarized cellular immune response, in which interferon-gamma and other proinflammatory cytokines activate the bactericidal machinery of infected macrophages [2]. Circulating Th1, Th2, Th17, and regulatory T-cell populations have been shown to shift characteristically during acute brucellosis [3], and elevated serum interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) have been repeatedly reported in acute disease, correlating with traditional inflammatory markers such as C-reactive protein (CRP) and declining after successful antimicrobial treatment [4-6].

In a large cohort from an endemic region of China, IL-6 and interferon-gamma levels were independently associated with disease severity, supporting their potential value as immunological markers of disease activity [7]. Despite this evidence base from other endemic regions, data on the acute-phase cytokine profile of brucellosis in Iraqi patients remain scarce. This short communication reports serum IL-6 and TNF- α levels in a cohort of Iraqi patients with acute brucellosis relative to healthy controls, and examines their correlation with CRP as a conventional marker of inflammatory activity.

2. Material and Methods

This case-control study was conducted at college of Science, Mustansiriyah University, Baghdad, Iraq. Forty patients with acute brucellosis, diagnosed on the basis of compatible clinical features together with a positive standard tube agglutination titer ($\geq 1/160$) and/or a positive blood culture for *Brucella* species, were enrolled, along with 30 age- and sex-matched healthy controls with no history of brucellosis or current febrile illness collected samples from Al Kindy teaching Hospital. Patients with chronic brucellosis (symptom duration > 3 months), other concurrent infections, autoimmune disease, or immunosuppressive therapy were excluded. The study protocol was approved by the Institutional Research Ethics Committee of the College of Science, Mustansiriyah University, and written informed consent was obtained from all participants.

Venous blood samples were collected prior to initiation of antimicrobial therapy, allowed to clot, and centrifuged to obtain serum, which was stored at -80°C until analysis. Serum IL-6 and TNF- α concentrations were measured using commercial sandwich ELISA kits according to the manufacturer's instructions, with results expressed in pg/mL. Serum CRP was measured by a standard turbidimetric assay. Between-group comparisons were performed using the independent-samples t-test or Mann-Whitney U test as appropriate, and correlations between cytokines and CRP were assessed using Pearson's or Spearman's correlation coefficient. A p-value < 0.05 was considered statistically significant.

3. Results

Patients with acute brucellosis had significantly higher serum IL-6 (38.6 ± 9.4 pg/mL vs. 6.2 ± 2.1 pg/mL, $p < 0.001$) and TNF- α (24.3 ± 6.1 pg/mL vs. 8.7 ± 2.4 pg/mL, $p < 0.001$) than healthy controls (Table 1, Figure 1). Serum CRP was likewise elevated in patients (34.2 ± 11.6 mg/L vs. 4.1 ± 1.8 mg/L, $p < 0.001$). Both IL-6 and TNF- α correlated positively with CRP (IL-6: $r = 0.61$, $p < 0.001$; TNF- α : $r = 0.54$, $p < 0.001$), consistent with a coordinated proinflammatory response during acute infection.

Table 1. Serum IL-6, TNF- α , and CRP levels in patients with acute brucellosis and healthy controls (mean $\pm$ SD).

Parameter	Patients (n=40)	Controls (n=30)	p-value
IL-6 (pg/mL)	38.6 $\pm$ 9.4	6.2 $\pm$ 2.1	<0.001
TNF- α (pg/mL)	24.3 $\pm$ 6.1	8.7 $\pm$ 2.4	<0.001
CRP (mg/L)	34.2 $\pm$ 11.6	4.1 $\pm$ 1.8	<0.001

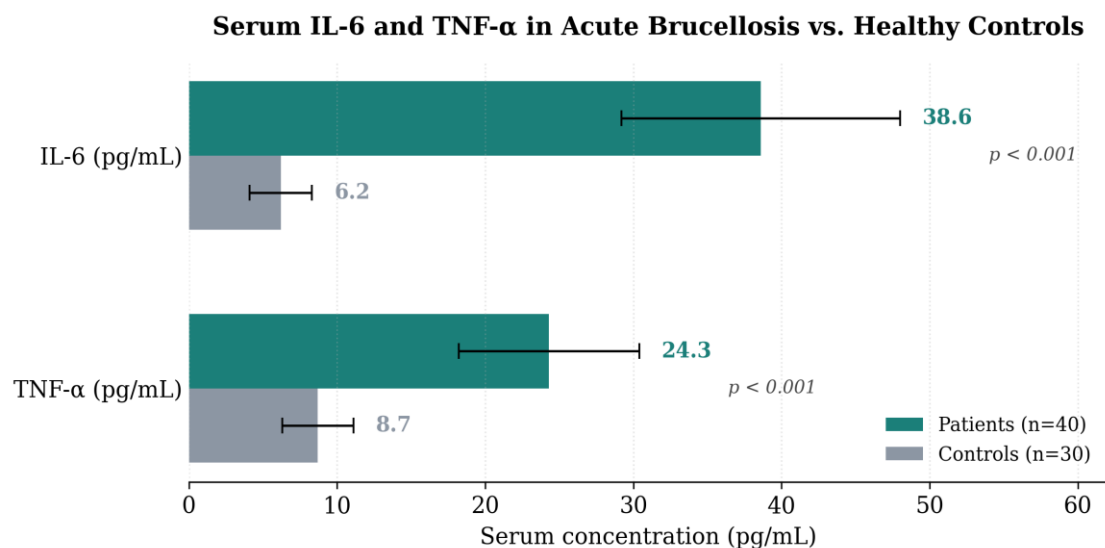


Figure 1. Serum IL-6 and TNF- α levels in patients with acute brucellosis versus healthy controls (mean $\pm$ SD). *** p < 0.001.

4. Discussion

The marked elevation of serum IL-6 and TNF- α observed in this Iraqi cohort is consistent with the proinflammatory, Th1-skewed cytokine profile repeatedly described in acute brucellosis in other endemic populations [4,5], and with reports linking IL-6 in particular to disease severity [7]. The positive correlation between both cytokines and CRP observed here mirrors the broader pattern by which IL-6 drives the hepatic acute-phase CRP response across bacterial infections [8], and is consistent with earlier work identifying CRP itself as a prognostic indicator that tracks disease evolution and treatment response in acute brucellosis [9]. This supports the interpretation that IL-6 and TNF- α are not isolated laboratory findings but part of a coordinated systemic inflammatory response to active *Brucella* infection, mirroring the role of Th1-derived cytokines in activating macrophage bactericidal mechanisms against this intracellular pathogen [2]. A similar IL-6-CRP relationship has also been reported in brucellosis presenting with reactive arthritis, further supporting IL-6 as a consistent correlate of inflammatory activity across clinical presentations of the disease [10].

Given their accessibility by standard ELISA and their strong correlation with a conventional inflammatory marker already used in clinical practice, serum IL-6 and TNF- α may hold practical value

as adjunct biomarkers of disease activity in acute brucellosis, particularly in endemic, resource-limited settings such as Iraq where more specialized immunological assays are not routinely available. As a short communication, this study is limited by its modest sample size, cross-sectional design, and the absence of longitudinal sampling to track cytokine kinetics with treatment response; larger prospective cohorts with post-treatment follow-up are needed to confirm the diagnostic and prognostic utility of these markers and to determine whether they outperform CRP as indicators of treatment response.

5. Conclusion

Acute brucellosis in this Iraqi cohort was associated with significant elevation of serum IL-6 and TNF- α , both correlating positively with CRP. These findings support a proinflammatory Th1-skewed immune signature in acute human brucellosis and suggest that serum IL-6 and TNF- α warrant further evaluation as accessible immunological markers of disease activity in endemic settings.

Acknowledgments: The authors would like to express many thanks to Mustansiriyah University, College of Science, Biology department, Baghdad, Iraq for their support to complete this work.

Conflict of interest statement: The authors declare no conflict of interest.

The Authors Involved in the Research: The Sawsan Mohammed Kareem ,Ammar Abbas Shalan ,Iman Ghanim ALRakh and Vikramsinh Bapurao More, contributed to the research design to analyze the results and write the manuscript, and the authors approved the final version for submission.

Data availability: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Consideration: The study was approved by Mustansiriyah University, Baghdad, Iraq.

Funding: No Funding.

References

1. Mohamed T, Yahya NB. Epidemiological analysis of childhood brucellosis in Duhok, Iraq: a retrospective observational study from 2018 to 2021. *Cureus*. 2024;16(7):e64934. <https://doi.org/10.7759/cureus.64934>
2. Oliveira SC. Host immune responses and pathogenesis to *Brucella* spp. infection. *Pathogens*. 2021;10(3):288. <https://doi.org/10.3390/pathogens10030288>
3. Zheng R, Xie S, Zhang Q, Cao L, Niyazi S, Lu X, et al. Circulating Th1, Th2, Th17, Treg, and PD-1 levels in patients with brucellosis. *J Immunol Res*. 2019;2019:3783209. <https://doi.org/10.1155/2019/3783209>

4. Demirdag K, Ozden M, Kalkan A, Godekmerdan A, Kilic SS. Serum cytokine levels in patients with acute brucellosis and their relation to the traditional inflammatory markers. *FEMS Immunol Med Microbiol.* 2003;39(2):149-53. [https://doi.org/10.1016/S0928-8244\(03\)00207-4](https://doi.org/10.1016/S0928-8244(03)00207-4)
5. Akbulut H, Celik I, Akbulut A. Cytokine levels in patients with brucellosis and their relations with the treatment. *Indian J Med Microbiol.* 2007;25(4):387-90. <https://doi.org/10.4103/0255-0857.37345>
6. Tang Y, Ma C, Sun H, Yang S, Yu F, Li X, et al. Serum levels of seven general cytokines in acute brucellosis before and after treatment. *Infect Drug Resist.* 2021;14:5501-10. <https://doi.org/10.2147/IDR.S341331>
7. Lin ZQ, Lin GY, He WW, Zhang C, Zhang R, Li YD, et al. IL-6 and INF- γ levels in patients with brucellosis in severe epidemic region, Xinjiang, China. *Infect Dis Poverty.* 2020;9(1):47. <https://doi.org/10.1186/s40249-020-00666-7>
8. Slaats J, ten Oever J, van de Veerdonk FL, Netea MG. IL-1 β /IL-6/CRP and IL-18/ferritin: distinct inflammatory programs in infections. *PLoS Pathog.* 2016;12(12):e1005973. <https://doi.org/10.1371/journal.ppat.1005973>
9. Navarro JM, Mendoza J, Leiva J, Rodríguez-Contreras R, de la Rosa M. C-reactive protein as a prognostic indicator in acute brucellosis. *Diagn Microbiol Infect Dis.* 1990;13(3):269-70. [https://doi.org/10.1016/0732-8893\(90\)90071-3](https://doi.org/10.1016/0732-8893(90)90071-3)
10. Noor K, Sami H, Khan PA, Sabir AB, Jilani LZ, Ahmad H, et al. Serum cytokine profiles and inflammatory markers in brucellosis-associated arthritis: a cross sectional study. *Zoonotic Dis.* 2026;6(2):16. <https://doi.org/10.3390/zoonoticdis6020016>

How to cite this article

Kareem SM, Shalan AA, AL-Rakh IG, More VB., Serum IL-6 and TNF- α as Early Immunological Biomarkers of Disease Activity in Acute Brucellosis. <i>Journal of Biomedicine and Biochemistry.</i> 2026;5(3):56-60. doi:10.57238/jbb.2026.7432.1182.
--