AMERICAN JOURNAL OF BIOLOGY AND NATURAL SCIENCES

https://biojournals.us/index.php/AJBNS

ISSN: 2997-7185

Article

Role of Interleukin-12 in Immune Response Polarization and Parasite Persistence in Cutaneous Leishmaniasis

Reham Firas Faris

Department of Biology, Collage of Science, Tikrit University ,Tikrit, Iraq

*Corresponding author E-mail: reham.fi.faris@tu.edu.iq

Citation: Faris, R. F. Role of Interleukin-12 in Immune Response Polarization and Parasite Persistence in Cutaneous Leishmaniasis. American Journal of Biology and Natural Sciences 2026, 3(4), 61-65

Received: 10th Jan 2026
Revised: 21th Feb 2026
Accepted: 14th Mar 2026
Published: 09th Apr 2026

Abstract: Cutaneous leishmaniasis is one of the parasitic diseases caused by Leishmania species and characterized by many symptoms, ranging from automatic lesion to chronic infection. Disease Development is mainly influenced by host–parasite interactions in addition to balance between cellular Immunological responses. The aim of current study is to examine the importance of interleukin-12 (IL-12) in regulating immune responses and its effect on parasite continuation in Subjects with cutaneous leishmaniasis. Total of 100 patients were grouped into three groups: individuals with self-healing, Chronic patients ,-healthy group as a control group. Levels of IL-12, interferon-gamma (IFN-γ), and interleukin-4 (IL-4) is serum were measured using ELISA, then statistical analyses were conducted using ANOVA then by Tukey's post-hoc test for multiple comparisons. The results have shown that patients who spontaneous healing show significantly higher levels of IL-12 and IFN-γ compared to both chronic cases and healthy controls, indicating a strong T helper 1 (Th1)-mediated immune response associated with effective parasite clearance. In contrast, chronic patients showed high levels of IL-4, suggesting a biased T-helper 2 (Th2) immune response that may Enhance parasite survival within host macrophages. These results highlight the critical role of IL-12 in controlling host immune responses and affecting disease result in cutaneous leishmaniasis. From a parasitological perspective, IL-12 may Play a role in enhancing intracellular parasite clearance and could act as a possible immunological biomarker for disease progression.

Keywords: Chronic infection; Cutaneous leishmaniasis; Cytokine profiling; Immune response; *Leishmania*; Parasite clearance; IL-12; Th1/Th2 polarization

Introduction

Cutaneous leishmaniasis is a parasitic infection resulting from species belonging to the genus *Leishmania*, which are intracellular protozoan parasites spread through the infected female sand-fly which grouped within Phlebotomus genus, which considered one of the major understudied tropical diseases, with high widespread in endemic regions such as in Iraq, Iran, Syria, and Afghanistan [1]. Clinically, the disease demonstrates a broad spectrum of manifestations, varying from localized lesions that may self-heal to chronic non-healing lesions that can remain for a long time [2].

From a parasitological perspective, the result of infection is not solely determined by the presence of the parasite but rather by the interaction between the parasite on one hand and the immune system in the host on the other. Leishmania have evolved advanced mechanisms that enable their survival within host macrophages, like modulation of host cell signaling pathways and avoidance of immune responses. The persistence of intracellular parasites is therefore a key factor contributing to disease chronic infection and therapeutic challenges [3].

Cell-mediated immunity plays an important role in control of Leishmania infection especially by the balance between immunological responses T-helper 1 (Th1) and T-helper 2 (Th2). Th1 responses are distinguished by the production of interferon-gamma (IFN-γ), which stimulates Phagocytes and improves their ability to get rid of cell-invading parasites. By contrast, Th2-responses are associated with secretion of cytokines such as interleukin-4 (IL-4) and interleukin-10 (IL-10), which reduces the effectiveness of cellular immunity and support parasite survival [4],[5].

Interleukin-12 (IL-12)-is considered an essential cytokine that regulates the immune system that operate the immune response to a Th1 phenotype, thereby stimulating IFN-γ production and enhancing macrophage activation. Many studies have showed that IL-12 have a important role in Defense to Leishmania infection and helps to parasite clearance in both experimental and in patients [6],[7]. Moreover, IL-12 administration has been shown to enhance disease results in animal models, showing its ability as an immunomodulatory factor [8],[9].

Despite these advances , region-specific studies that studying cytokine profiles between Iraqi patients with cutaneous leishmaniasis still limited , specially in some endemic areas such as Salah al-Din city. A clearer understanding of the relationship between cytokine balance and clinical symptoms may yield useful information for host–parasite interactions and disease progression[10]. Therefore, the study aims to evaluate levels of IFN-γ, IL-12, and IL-4 in the patients with cutaneous leishmaniasis and to discuss their association with disease result , with particular emphasis on parasite persistence and immune response polarization.

Materials and Methods

1. Study methodology

The aim was to design a cross-sectional investigation conducted in Salah al-Din city-Iraq, from January and to 2025.Study area included Tikrit city and its surrounding regions. The primary objective was to examine the relationship between cytokine levels and clinical outcomes of cutaneous leishmaniasis, with particular Focus on host–parasite interactions and patterns of immune response.

2. Sample collection

Total of 100 samples have been collected and divided into three groups as follows:

1. Patients with cutaneous leishmaniasis demonstrating self-healing (n = 30)
2. Patients with chronic cutaneous leishmaniasis (n = 30)
3. Healthy control group (n = 40)

Table 1. Distribution of participants by clinical status

Group	Number of samples	Sample percentage (%)
Leishmaniasis patients - self-healing	**30**	**30%**
Leishmaniasis patients - chronic cases	**30**	**30%**
Control group (healthy)	**40**	**40%**
Total	**100**	**100%**

Participants were selected using a convenience sampling approach from individuals attending local healthcare centers in Tikrit and nearby areas. Individuals with known chronic systemic diseases or immunological disorders were excluded in order to minimize potential confounding factors and ensure homogeneity among the study groups.

3. Diagnostic Criteria and Classification

Cutaneous leishmaniasis was confirmed with clinical evaluation performed by a dermatologist , in addition to parasitological proof through microscopic examination of Giemsa-stained skin smears. patients were further classified into spontaneous healing and chronic forms according to disease duration, number of lesions, and response to previous treatment (complete or partial healing).

4. Sample Collection and Processing

Blood samples were collected (approximately 5 ml) then samples were allowed to clot at room temperature .Samples were separated at 3000 rpm for 10 minutes to separate the serum . The separated serum was grouped into smaller portions and stored at −20°C until further analysis.

5. Cytokine Measurement

Serum levels of IFN-γ, IL-12, and IL-4 have been measured with ELISA--kits (from R & D Systems, Minneapolis, USA) following the manufacturer's-instructions. All experimental measurements were performed in the Microbiology Laboratory, College of Medicine, Tikrit University.

6. Statistical Analysis

Statistical software SPSS version25 >was used to analyze data. Descriptive statistics were presente as mean ± standard-deviation (mean ± SD) and the differences between groups were analyzed=using one way analysis of7variance (ANOVA), followed by Tukey's HSD test to compare several groups. P-value below 0.05 has taken as an indicator of statisticalhsignificance.

Result and Discussions

Result

1. Cytokine Profiles Among Study Groups

Levels of IL-12, IFN-γ, and IL-4 in serum have been measured in the three study groups : 1-self-healing patients 2- chronic cases 3- healthy controls. The results revealed significant differences in cytokine levels among the groups ($p < 0.05$).

Table 2. Serum cytokine levels in study groups (Mean ± SD)

Group	IL-4 (pg./mL)	IFN-γ (pg./mL)	IL-12 (pg./mL)
Self-healing patients	20 ± 6	150 ± 18	120 ± 15
Chronic patients	35 ± 8	80 ± 12	45 ± 10
Healthy controls	40 ± 7	70 ± 9	40 ± 8

2. Interleukin-12 (IL-12)

The level of IL-12 in Self-healing group patients has shown a significantly higher meean level of IL-12 (120 ± 15 pg/mL) compared to chronic patients (45 ± 10 pg/mL) and healthy controls (40 ± 8 pg/mL). Post hoc analysis confirmedthat the results showed significant differences ($p < 0.05$)

3. Interferon-gamma (IFN-γ)

Similarly, IFN-γ levels were significantlly higher in self-healing patients group (150 ± 18 pg/mL), whereas chronic patients (80 ± 12 pg/mL) and controls (70 ± 9 pg/mL) showed lower levels. This indicates that activation of a Th1-mediated immune response in the self-healing group.

4. Interleukin-4 (IL-4)

In contrast, IL-4 levels were significantly higher in chronic patients (35 ± 8 pg/mL) compared to self-healing patients (20 ± 6 pg/mL), with the highest levels observed in healthy controls (40 ± 7 pg/mL). This pattern suggests a shift toward a Th2-type immune response in chronic infection.

5. Comparative Analysis

One-way ANOVA have shown significant differences between all groups for the three cytokines studied ($p < 0.05$). Tukey's HSD post hoc test indicated that the most clear differences were seen between self-healing and chronic patients, particularly for IL-12 and IFN-γ.

Discussion

These results have shown a clear relationship between cytokine profiles and disease outcome in cutaneous leishmaniasis, indicating the importance of host–parasite interactions in determining infection progression.

From a parasitological perspective, the elevated levels oflIL-12 and IFN-γ observed in self-healing patients indicate an effective Th1-mediated immune response, which is crucial for activating macrophages and promoting intracellular clearance of Leishmania amastigotes. These results are in agreement with studies that emphasize the important role of IL-12 in inducing IFN-γ production and enhancing parasite clearance [11],[12],[6].

In contrast, chronic patients exhibited significantly lower IL-12 and IFN-γ levels, accompanied by elevated IL-4. This cytokine profile reflects a shift toward a Th2-dominated immune response, which is less effective in controlling intracellular parasites. The persistence of Leishmania in such cases can be attributed to the parasite's capacity to survive within macrophages through modulation of host immune signaling pathways and inhibition of effective cellular responses.

The increased IL-4 levels observed in chronic infection may also enhance alternative macrophage activation (M2 phenotype) which helps the parasite survive instead of being eliminated . This agrees with previous results indicating that IL-4 helps to disease progression by inhibiting Th1 responses [13],[14][15].

Notably the healthy controls showed relatively higher IL-4 levels compared to self-healing patients, which may show normal immune regulation instead of responses triggered by infection. However, the absence of elevated IL-12 and IFN-γ in this group confirms the lack of active cellular immune stimulation against the parasite.

The results from this study enhance the concept that disease effect in cutaneous leishmaniasis is strongly influenced by the equilibrium between Th1 and Th2 responses. A dominant Th1 response is associated with parasite clearance and lesion healing, whereas a Th2-skewed response contributes to parasite persistence and chronic disease. From a clinical and parasitological perspective IL-12 may plays as a useful-indicator of effective immune response and can play a role in guiding immunotherapeutic strategies aimed at enhancing parasite elimination.

Conclusion

Thus, this paper demonstrates that IL-12 is critical for immune response polarization and disease outcomes in cutaneous leishmaniasis. The results show that high IL-12 and interferon-gamma (IFN-γ) levels among self-resolving patients are highly associated with a protective Th1 immune response leading to efficient parasite clearance and, conversely, low IL-12 and higher interleukin-4 (IL-4) levels in chronic cases are compatible with a supportive Th2-skewed immune response that permits parasite survival. The current findings highlighted the critical cytokine balance in host–parasite interactions and validated IL-12 as a major immunological determinant that dictates the course of disease. These findings have important clinical and parasitological implications and may represent an opportunity for IL-12 to be used as a potential prognostic biomarker of disease and as a target for immunotherapeutic approaches aimed at bolstering host resistance and improving disease outcomes. In addition, the study gives regional data that provides more insight on immune dynamics in endemic regions. Longitudinal studies necessary to validate IL-12 as a predictive biomarker, therapeutic applications of IL-12 cytokines-based treatment and identification and characterization of additional immune mediators involved in parasite persistence in humans and animal models to devise more effective and targeted strategies to combat cutaneous leishmaniasis.

REFERENCES

[1] J. Alvar, I. D. Vélez, C. Bern, M. Herrero, P. Desjeux, J. Cano, et al., "Leishmaniasis worldwide and global estimates of its incidence," PLOS ONE, vol. 7, no. 5, p. e35671, 2012.

[2] H. J. C. De Vries, H. D. F. H. Schallig, and S. H. Reedijk, "Cutaneous leishmaniasis: A 2022 updated narrative review into diagnosis and management developments," American Journal of Clinical Dermatology, vol. 23, no. 6, pp. 823–840, 2022, doi: 10.1007/s40257-022-00726-8.

[3] G. A. Duque and A. Descoteaux, "Leishmania survival in the macrophage: Where the ends justify the means," Current Opinion in Microbiology, vol. 26, pp. 32–40, 2015.
[4] J. Alexander and K. Bryson, "T helper cell bias in leishmaniasis," Current Opinion in Immunology, vol. 17, no. 4, pp. 421–426, 2005.
[5] N. Maspi et al., "Pathogenesis of cutaneous leishmaniasis," Journal of Immunology Research, vol. 2016, p. 8174745, 2016.
[6] S. Farajnia et al., "Immunomodulatory effects of IL-12 in leishmaniasis: A review," Immunology Letters, vol. 245, pp. 15–23, 2022.
[7] P. H. van der Meide et al., "IL-12 and IL-23 in parasite immunity," Frontiers in Immunology, vol. 6, p. 303, 2015.
[8] A. Miramin-Mohammadi, A. Javadi, S. E. Eskandari, H. Mortazavi, M. N. Rostami, and A. Khamesipour, "Immune response in cutaneous leishmaniasis patients with healing vs. non-healing lesions," Iranian Journal of Microbiology, vol. 12, no. 3, p. 249, 2020.
[9] H. W. Murray et al., "Advances in leishmaniasis treatment," Trends in Parasitology, vol. 21, no. 11, pp. 508–512, 2005.
[10] P. Kaye and P. Scott, "Leishmaniasis: Complexity at the host–pathogen interface," Nature Reviews Microbiology, vol. 9, no. 8, pp. 604–615, 2011, doi: 10.1038/nrmicro2608.
[11] C. Bogdan, "The function of nitric oxide in the immune system," Current Opinion in Immunology, vol. 8, no. 1, pp. 64–70, 1996.
[12] J. E. Uzonna, K. L. Joyce, and P. Scott, "Low dose Leishmania major promotes a transient T helper cell type 2 response that is down-regulated by interferon γ-producing CD8+ T cells," The Journal of Experimental Medicine, vol. 199, no. 11, pp. 1559–1566, 2004, doi: 10.1084/jem.20040172.
[13] D. Sacks and N. Noben-Trauth, "Susceptibility to Leishmania major," Nature Reviews Immunology, vol. 2, no. 11, pp. 845–858, 2002.
[14] S. L. Reiner and R. M. Locksley, "Regulation of immunity to Leishmania major," Annual Review of Immunology, vol. 13, no. 1, pp. 151–177, 1995.
[15] World Health Organization, "Leishmaniasis," 2023. [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/leishmaniasis