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Assessing Cytokines and Immunoglobulins (IgG subclass) Markers in Cutaneous Leishmaniasis Infections

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ABSTRACT

Understanding the interaction between cytokines and immunoglobulins in immune responses to infection is crucial for elucidating the mechanisms of immunity and developing diagnostic biomarkers. This study aimed to assess the levels of key cytokines (IFN-γ, IL-4, IL-10, IL-17) and immunoglobulin IgG and its subclasses (IgG1–4) in cutaneous leishmaniasis-infected and non-infected individuals, stratified by gender, age, and clinical status. A cross-sectional study was conducted among 104 individuals with cutaneous leishmaniasis (52 males and 52 females). Immunoglobulins and IFN-γ, IL-4, IL-10, and IL-17 were measured by ELISA. Statistical analyses included mean comparisons (T-test, ANOVA), standard deviations, and correlation coefficients. Significant differences were noted in IFN-γ ($p = 0.025$), IgG1 ($p = 0.011$), and IgG4 ($p = 0.02$) levels between infected and non-infected groups. Sex-specific variations were observed, with higher IgG3 in males ($p = 0.034$) and elevated IL-10 in females ($p = 0.024$). Strong correlations were detected between IL-4 and IgG1 ($r = 0.77$, $p < 0.01$) and between IL-10 and IgG1 ($r = 0.86$, $p < 0.01$). This study highlights the dynamic relationship between humoral and cellular immune markers, suggesting their potential as biomarkers for stratifying infection. Sex significantly affects these profiles, confirming the need for personalized immunological assessments.

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1. INTRODUCTION

Baghdad boil or Cutaneous leishmaniasis (CL) is a parasitic dermatosis caused by a flagellated protozoan Leishmania genus. It is characterized by the lesion resulting from the bite of the sand fly, which injects the promastigote, which are quickly taken up by the phagocytic cells, causing, after multiplying inside these cells, the explosion of the infected cells and the release of the parasites that infect new cells, causing the appearance of the lesion [1]. This disease is distinguished by a complex immune response that interacts with the parasite and affects its persistence. The humoral and cellular immune systems play pivotal roles in the progression of disease and its clinical presentation [1], [2]. Humoral immunity is focused on antibodies, which are produced by B cells. These antibodies bind to foreign cells or substances to reduce their effect or activate other cells to attack them. They also activate the complement system to increase the elimination of microbes [3]. The most abundant immunoglobulins in serum and is IgG antibody, and its substantial in mediating immune responses against Leishmania parasites [4]. Immunoglobulin G (IgG) and its sub-classes (IgG1, IgG2, IgG3, IgG4) exhibit distinguished effector functions, with IgG1 and IgG3 correlated with pro-inflammatory responses, while IgG2 and IgG4 are associated with immune regulation. Previous study has shown that IgG levels, essentially IgG1 and IgG2 sub-classes, are rising in CL patients, reflecting their participation in parasite control [4],[5]. IgG1 is related with a Th2-type immune response, which may associate with disease susceptibility, whereas IgG2 is linked to a Th1 response, supporting parasite clearance [6] Previous research has found critical variations in seroprevalence IgG subclass among cutaneous leishmaniasis patients, suggesting possible biomarkers for disease severity and immune protection [7].

It is well known that the main defense mechanism against intracellular agents, such as leishmaniasis, is generally associated with the activation of cellular immunity by Th1 cytokines, such as INF-γ, TNF-α, and IL-12 [8].

Cytokines such as IL-4, IL-10, IL-17, and IFN-γ involve in the immune response in CL. IFN-γ stimulate a protective Th1 response, whereas IL-4 and IL-10 boost Th2 and regulatory responses, possibly facilitating parasite survival. IL-17 participates in neutrophil recruitment and induce inflammation, which may exacerbate the damage of tissue. The equilibrium between these cytokines' influences switching of IgG subclass, yet the accurate relationships in CL remain unclear [9], [10]. The clinical outcome of CL depends on the host immune response, where cytokines play a pivotal role in modulating disease progression, parasite clearance, and tissue pathology. Key cytokines, including interleukin-4 (IL-4), interleukin-10 (IL-10), interleukin-17 (IL-17), and interferon-gamma (IFN-γ), determine the balance between protective immunity and immunopathology [11], [12]. IFN-γ, a Th1 cytokine, is crucial for macrophage activation and intracellular parasite killing, driving protective immunity against Leishmania [13]. However, its efficacy can be counteracted by immunosuppressive cytokines such as IL-4 and IL-10, which promote Th2 responses and facilitate parasite survival [14] It has reported elevated IL-10 levels in CL patients, correlating with chronicity and delayed healing [15]. Meanwhile, IL-17, a pro-inflammatory cytokine linked to neutrophil recruitment, has been associated with both protective and pathological roles in CL, depending on disease stage and Leishmania species [11].

This study examines the levels of IgG subclasses (IgG1, IgG2, IgG3, IgG4) and cytokines (IL-4, IL-10, IL-17, IFN-γ) in patients of CL, exploring the correlations among them and their associations with disease severity by Compare cytokine/IgG profiles between CL patients and endemic controls. Assess sex- and age-related immunological variations. Identify biomarker candidates via correlation networks. Understanding these interplays may provide insights into immune polarization in CL and identify possible biomarkers for disease progression or therapeutic targets.

2. Experimental Methodology

This study was conducted as a laboratory analytical study aimed to evaluate the levels of some immune markers: IL-4, IL-10, IL-17, Ig-1, IgG2, IgG3, IgG4, and INF-γ in individuals with cutaneous leishmaniasis.

2.1 Sample collection and Diagnosis.

Attending patients at the laboratory of Baqubah Teaching Hospital, of all ages and both sexes with clinically suspected CL lesions, were examined to detect infection from 1st October, 2024 to 1st March, 2025. A total of 320 patients were examined using suspected sampling. Demographic and clinical information was written down using a standardized questionnaire that included age, sex, residence, and lesion features (number, type, location, and period) for 104 patients (52 males and 52 females) after confirmation of the infection with leishmaniasis by microscopic examination. With a note that all patients in this study were attending the hospital for the first time and had not yet received treatment. Patients who had been treated once or more were excluded. The study included 40 blood samples drawn from healthy individuals as controls, with 20 male and 20 female samples. They were confirmed to be free of parasitic infections, chronic diseases, and other illnesses.

Ethical approval for the study was obtained from the Ethics Committee of the University of Diyala, College of Education for Pure Sciences (Ref: CEPEC/011: 2024-09-17). Written consent was obtained from all participants or their parents.

2.2 Immunoglobulins and Cytokines Testing

104 blood samples, in addition to 40 blood control samples, were collected and placed in clean tubes. The blood was centrifuged at 3000 rpm for 10 minutes. The serum samples were stored at -20°C until analysis.

Prepared ELISA kits were used to determine the levels of the following immune markers:

1. Interleukin-4 (IL-4), IL-10, and IL-17, as an indicator of Th2 immune response activity, was measured using a Biotic ELISA kit from the country of origin (China).
2. Human Immunoglobulin G1, G2, G3 (IgG1, IgG3, IgG3, IgG4), to detect immunity using a Biotic ELISA kit from the country of origin (China).
3. Interferon-γ (INF-γ), an indicator of Th1 cellular response, was determined using a Biotic ELISA kit from the country of origin (China).

These steps were carried out according to the manufacturer's instructions, and the absorbance was read using an ELISA reader at the appropriate wavelength (450 nm).

2.3 Data analysis

Data were analyzed using SPSS v26.0. A t-test was conducted to compare the mean concentrations and standard deviations of cytokines and immunoglobulins between CL-positive and non-infected individuals, and correlation coefficients were assessed. *p*-values <0.05 were considered significant.

3. RESULTS AND DISCUSSION

3.1 Comparison of immunological biomarkers according to sex

In Table 1, the immunological biomarkers between individuals with cutaneous leishmaniasis and non-infected individuals were compared by sex (males and females). It was shown that IgG1 was higher in both infected males and females compared with non-infected individuals (4.2113±0.0121, 3.576±0.2215 vs 1.345±0.8823, 0.6363±0.1154, respectively), with significant differences. In the same table, IgG4 was higher in both infected males and females than in non- infected (237.9897±0.0214, 316.2214±0.546 vs 61.834±0.7721, 48.5640±1.287, respectively). There was a significant difference. For the cytokines IL-4, IL-10, IL-17, and INF-γ, all showed significant differences ($p < 0.05$) between infected and non-infected groups in both sexes, with higher concentrations in infected individuals. As these results indicate, infection with Baghdad boil significantly alters IgG subtypes and cytokine levels, with more pronounced effects in males for some biomarkers (e.g., IgG1).

Table 1: Comparison of the immunological biomarkers between individuals infected with cutaneous leishmaniasis and non-Infected individuals according to Sex (males and females).

Groups	Infected		Not infected			Infected		Not infected		
Sex	Males(52)		Males(20)		P.value	Females(52)		Females(20)		P.value
Concentrations	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
IgG1	4.2113	0.0121	1.345	0.8823	0.001	3.576	0.2215	0.6363	0.1154	0.011
IgG2	16.6543	0.0331	10.4325	0.8843	0.03	24.1654	1.115	12.3960	1.0021	0.037
IgG3	139.7798	0.0213	112,165	0.7765	0.01	133.2165	0.465	146.9600	0.023	0.034
IgG4	237.9897	0.0214	61,834	0.7721	0.002	316.2214	0.546	48.5640	1.287	0.02
IL-4	23.5421	0.2576	14.3321	0.9923	0.013	33.3765	0.6613	17.2543	1.0014	0.01
IL-10	18,123	0.41335	11,325	0.92213	0.024	16,657	1.637	15.9547	0.526	0.011
IL-17	18.7761	0.2214	18,154	0.2765	0.014	27.8756	0.0134	21.1337	0.0024	0023
INF-γ	91.5478	0.0243	26,376	0.5768	0.02	103.3354	0.7689	20.1163	2.576	0.025

Cutaneous leishmaniasis induce complex immune response that correlate with it has survive in host and /or control the disease. In this study, all IgG1, IgG2, IgG3 and IgG4 Significantly higher in infected individuals (both sexes except IgG3 was decrease in females) compared to non-infected controls, with IgG4 levels notably elevated in females, which agree with [7], and [16]. Noted that all IgG subclass were higher in all type of cutaneous leishmaniasis and they reported that IgG2 was characteristic of DL [7], [16]. This result disagrees with [17]. Who obtained that no significance changes of immunoglobulin levels in patients with cutaneous leishmaniosis [17]. The differences in the method of measuring immunoglobulins may be the reason for this discrepancy in the result. The rise of IgG subclass suggests a robust humoral response, particularly IgG4, which is associated with immune regulation and chronicity. Cytokines (IL-4, IL-10, IL-17, IFN-γ), all were significantly elevated in infected individuals, indicating a mixed Th1/Th2/Th17 response. IFN-γ (Th1) was higher in males, aligning with stronger cellular immunity, while IL-10 (immunosuppressive) was higher in females, potentially contributing to sex-based differences in disease progression [18], [19].

Males showed higher IgG3 (pro-inflammatory), while females had elevated IL-10, suggesting hormonal or genetic influences on immune polarization. This increase also constituted a significant difference, because the increase in IgG in those infected with cutaneous leishmaniasis results from the activation of immunity against parasites, which indicates that the body can recognize the parasite and respond to it as well. Elevated IgG4 in females could indicate a regulatory response that might prolong parasite persistence, while higher IFN-γ in males correlates with better parasite control. The findings highlight sex-specific immune responses, which may explain variations in CL severity and healing rates between genders. This is not significant, as the body

successfully eliminates the parasite, and it may sometimes indicate a weakness in the cellular immune response, which is consistent with the study [4].

3.2 Comparison of immunological biomarkers according to lesion type:

Table 2 in this table it was compared the biomarker concentrations based on lesion type (dry and wet, moist, dry). In the current results IgG1 was higher in all infected individuals compared to non -infected and seems that those with both dry and wet and only wet cutaneous leishmaniasis lesions were higher than those with dry and not infected individuals (10.1000±0.321, 2.5568±1.32512 vs 2.05887±1.7421, 1.1310± 0.78066, respectively) with significant tendency to those with dry and wet lesions. IgG4 was higher in individuals with all types of lesions, tend to be highest in those with dry - wet lesions compared to others groups of lesions and compared to control as shown in table 2. Regarding to IL-4, IL-10, and IL-17, all showed a significant increase in infected individuals compared to non-infected except INF-γ, which had an insignificant increase (Table2).

Table (2) Comparison the immunological biomarkers between Infected with cutaneous leishmaniasis and non-Infected individuals according to Lesion type

Groups	Infected(No)		P.	Infected(No)		P	Infected(No))		Not -infected		P
	Dry(38)		value	Wet(35)		.value	Dry and Wet(31)				value
Concen	Mean	SD		Mean	SD		Mean	SD	Mean	SD	
IgG1	2.05887	1.7421	0.011	2.5568	1.32512	0.028	10.1000	0.321	1.1310	0.78066	0.025
IgG2	16.0661	1.4657	0.032	16.4229	0.41270	0.011	30.9051	1.387	12.6158	1.325	0.012
IgG3	140.2381	0.03438	0.013	115.9179	1.476	0.012	204.4855	1.267	138.2458	1.36	0.013
IgG4	200.4250	1.20276	0.027	214.9991	0.245	0.014	811.7928	0.4365	58.1700	1.165	0.033
IL-4	25.9793	0.15764	0.012	54,521	0.365	0.031	25.4065	1.3571	8.5471	1.1562	0.024
IL-10	10.1883	0.5732	0.032	16.0635	1.83543	0.011	18.3976	1.59550	14.1804	1.2662	0.011
IL-17	19.1927	1.487	0.024	17.9179	1.276	0.032	29.7321	0.43857	10.6436	1.3765	0.015
INF-γ	75.8703	0.40117	0.174	90.9233	2.376	0.098	220.5779	0.423	27.3175	1.4987	0.087

IgG1 and IgG4 were highest in individuals with dry-wet lesions, suggesting these lesion types trigger a stronger humoral response. IgG4 levels were strikingly high in dry-wet lesions, which may be tied to the chronicity of inflammation, suggesting a robust antibody response. This immune response, while strong, doesn't effectively eliminate the parasite. IL-4, IL-10, and IL-17 were significantly elevated in infected individuals, with IL-17 highest in wet lesions, this may point to implicate neutrophil involvement in the inflammatory process of these lesions and its significant role of neutrophil in pathogenesis of this lesion type [20] IFN-γ showed an insignificant increase, may reflect potential suppression in certain lesion types and this may aiding survive of parasites the result agrees with Piyasiri *et al.* [21].

Lesion-Specific Patterns were observed, with patients with Dry-wet lesions showing the most pronounced immune activation, possibly due to prolonged antigen exposure or infection with both lesion types, reflecting variation in parasite genera [22]. Lesion type influences immune polarization, with wet lesions associated with Th17/neutrophil responses and dry-wet lesions with regulatory (IgG4/IL-10) responses. IL-4 and IL-10 are also found in increased levels in infected individuals, contributing to the development of regulatory immune responses, especially in dry-wet lesions [23]. A weak or insignificant increase in IFN-γ, particularly in wet lesions, suggests local immune suppression that could be detrimental to the host and harmful to parasite survival.

3.3 Comparison of cytokines by infection acquisition date:

Table 3 compares biomarker concentrations by history of infection acquisition (Month, 2 months, more than 2 months). IgG1 and IgG4 were decreased as the infection period increased, and conversely, IgG2 increased as the period of infection increased, as shown in Table 3. IgG 3 was higher in individuals who acquired the infection for two months. All infected individuals had higher levels of all IgG subclasses than the control group. For IL-4, IL-10, IL-17, and INF-γ, all showed a significant increase in infected individuals compared to non-infected, with a tendency to be higher in those infected two months earlier, especially for IL-4, IL-10, and INF-γ, compared to the other two infected groups at $p \leq 0.05$ (Table 3).

IgG1 and IgG4 decreased with longer duration of infection, while IgG2 increased. IgG3 peaked at 2 months, suggesting temporal alternation in antibody profiles. This agrees with Anam *et al.* [24] while disagreeing with Solano-Gallego et al. [25], it may reflect a decline in their ability to fight the Leishmania parasite or parasite evasion mechanisms, or it may refer to healing [24], [25], [26]. IL-4, IL-10, and IFN-γ were highest at 2 months, referring to a peak in immune activity during this period, which agrees with Taheri et al. [27]. IL-17 remained elevated across all stages, which agrees with Morales-Primo *et al*. [28], who reported that

Th17 cell activities and synergies are critical for resistance to infection during the early and acute stages; however, Th17 cells might lead to a chronic stage [28]. Early infection (1 month) resulted in strong Th1 (IFN-γ) and Th2 (IL-4) responses, while chronic infection (>2 months) was characterized by declining IgG1/IgG4 but sustained IL-10. The 2-month mark may represent a crucial window for immune interference, as both pro-inflammatory (IFN-γ) and regulatory (IL-10) responses are active [27]. Declining IgG1/IgG4 over time may reflect immune exhaustion or parasite evasion mechanisms [24].

Table (3) Comparison the immunological biomarkers between Infected with cutaneous leishmaniasis and non-Infected individuals according to acquired 1st infection

Groups	Infected		p-value	Infected		p-value	Infected		Not infected		p-value
Acquired 1st infection	Month(54)			Two months (38)			More than 2 months(12)				
..Con	Mean	SD		Mean	SD		Mean	SD	Mean	SD	
IgG1	4.6262	0.0629	0.025	2.2343	1.325	0.013	1.3201	0.9293	1.1310	0.78066	0.034
IgG2	15.9776	1.325	0.025	18.6070	1.687	0.011	25.6921	2.0832	12.6158	1.325	0.032
IgG3	133.061	1.42	0.013	145.370	0.657	0.015	112.485	1.8964	138.246	1.36	0.042
IgG4	308.377	1.43	0.044	260.341	1.657	0.013	35.6623	1.9390	58.1700	1.165	0.013
IL-4	28.7050	1.13	0.054	255.162	1.36	0.014	21.7691	1.6348	8.5471	1.1562	0.011
IL-10	14.3974	1.3206	0.022	215.275	1.520	0.013	11.0601	1.0081	14.1804	1.2662	0.016
IL-17	19.2800	1.3292	0.014	13.9134	0.932	0.024	17.2893	1.6566	10.6436	1.3765	0.014
INF-γ	85,224	0.2143	0.011	117.076	1.354	0.027	105.736	1.4990	27.3175	1.4987	0.013

3.4 Comparison of immunological biomarkers concentrations regarding to location of lesions

To compare the mean concentrations of studied immunological biomarkers Table (4), based on the location of the lesion, in infected individuals with those are non-infected it was observed that IgG1 was higher in those infected in their faces and hands and legs compared with non-infected persons with non-significant increase. IgG2 was non-significant increase in all infected groups (in their hands, legs and faces) compared to non-infected, IgG3 was decrease in all groups of infected individuals regarding to location of lesion compared to non-infected, it was higher in those with lesion on their hands followed by those with lesion on their legs, while regarding to IgG4 the highest mean of concentration was recorded in those with lesion on their legs followed by those with lesion on their hands. IL-4, IL-10 and IL-17 was higher in those infected in their face compared to other location. INF-γ was higher in those with lesion on their hands. All markers were non significantly higher in infected individuals than control individuals.

Table (4): Comparison the immunological biomarkers between Infected with cutaneous leishmaniasis and non-Infected individuals according to Location of Lesions

Location of Lesions	Hands Mean Concentration –SD			Legs Mean Concentration -SD			Face Concentration - SD		control Mean Concentration – SD		
Concentration	Mean	SD	p-value	Mean	SD	p-value	Mean	SD	Mean	SD	p-value
IgG1	3,546	1.325	0.435	1.768	1.365	0.546	55,435	1.90353	1.1310	0.78066	0.26
IgG2	19.9400	1.325	0.576	13.3259	1.354	0.743	46,465	1.657	12.6158	1.325	0.165
IgG3	133.7618	1.436	0.776	106.605	0.243	0.423	36,132	0.95351	138.246	1.36	0.834
IgG4	215.7604	0.2876	0.436	470.137	0,356	0.923	54,255	0.88451	58.1700	1.165	0.445
IL-4	29.7278	1.3765	0.734	33.8597	1.546	0.534	46,335	1.265	8.5471	1.1562	0.287

IL-10	13.2873	1.543	0.734	9.8914	1.345	0.45	57,687	1.43528	14.1804	1.2662	0.843
IL-17	22.1480	1.576	0.354	12.8162	1.3245	0.423	67,165	1.77805	10.6436	1.3765	0.32
INF-γ	232.1755	1.786	0.026	95.6984	1.214	0.02	94,376	1.76951	27.3175	1.4987	0.01

IgG1 and IgG4 were highest in patient with facial and leg lesions, respectively. IgG3 was declined in all infected groups, suggesting localized suppression. Patients with facial lesions had the highest IL-4, IL-10, and IL-17, while IFN-γ was dominant in patients with hand lesions. Most biomarkers did not reach significance, possibly due to small sample sizes or high variability. However, facial lesions may drive stronger regulatory (IL-10) and Th2 (IL-4) responses, possibly linked to mucosal immune pathways. Hand lesions' high IFN-γ levels align with improve parasite control, possibly due to strong cellular immunity in these areas [29].

3.5 Comparison the immunological biomarkers between Infected with cutaneous leishmaniasis and non-Infected individuals according to numbers of lesions:

Regarding to compare between infected with cutaneous leishmaniasis and non-Infected individuals according to numbers of lesions, persons with one lesion occurred highest level for IgG2, IL-17 and INF-γ (19.9400 ±0.234, 22.1480 ±1.324 and 101.1755±1,234 respectively) as showed in Table 5, while IL-4 and IgG4 were increase in those with two lesions (470.137±0.25393 and 33.8597± 1.66576 respectively). For IgG1, IgG3 and IL-10, the highest level was in those with multiple lesions (3.7788±0.90353, 148.833±0.95351 and 15.7191±0.43528, respectively), all immunological biomarkers were higher in infected groups compared to control.

Table (5): Comparison the immunological biomarkers between Infected with cutaneous leishmaniasis and non-Infected individuals according to numbersof lesions

Groups	Infected								Non-infected		
No. lesions	one		P-value	two		P-value	Multiple		Non-infected		P-value
Concentrations	Mean	SD		Mean	SD		Mean	SD	Mean	SD	
IgG1	2.6847	1.232	0.230	1.5704	1.97632	0.654	3.7788	0.90353	1.1310	0.78066	0.29
IgG2	19.9400	0.234	0.324	13.326	1.90269	0.432	17.4283	1.63707	12.6158	1.325	0.427
IgG3	133.7618	1.443	0.324	106.605	0.82219	0.645	148.833	0.95351	138.246	1.36	0.836
IgG4	215.7604	0.432	0.123	470.137	0.25393	0.432	234.645	1.88451	58.1700	1.165	0.306
IL-4	29.7278	1.434	0.324	33.8597	1.66576	0.435	18.2019	1.26937	8.5471	1.1562	0.812
IL-10	13.2873	1.324	0.132	9.8914	1.99947	0.214	15.7191	0.43528	14.1804	1.2662	0.892
IL-17	22.1480	1.324	0.324	12.8162	0.10388	0.654	20.1294	1.77805	10.6436	1.3765	0.652
INF-γ	101.1755	1.234	0.213	95.6984	1.21340	0.546	94.3191	1.76951	27.3175	1.4987	0.24

IgG2, IL-17, IFN-γ occurred highest in patients with single lesions, suggesting a focused, effective immune response. IgG4 and IL-4 were elevated in patients with multiple lesions, indicating an alteration toward regulatory mechanisms as disease burden increases (number of lesions). IgG3 and IL-10 reached to its peak in multiple lesions, linking with chronicity and immune dysregulation. Single lesions may represent controlled Leishmania infections with strong Th1/Th17 responses, while multiple lesions reflect immune modulation (high IgG4/IL-10) and poorer outcomes (worst clinical features). Disease burden (lesion number) directly affects immune polarization [16].

3.6 Correlation

Strong correlations were detected between IL-4 and IgG1 ($r = 0.77$, $p < 0.01$) and between IL-10 and IgG1 ($r = 0.86$, $p < 0.01$) as shown in Table 6.

Table (6): Correlation Coefficient among IgG subclass and IL-4, IL-10, IL-17 and INFγ

	IgG4	IgG3	IgG2	IgG1
IL-4	0.74**	0.68*	0.69*	0.77**
IL-10	0.71**	0.77**	0.71**	0.86**
IL-17	0.68*	0.74**	0.74**	0.74**
INF-γ	0.73**	0.74**	0.76**	0.75**

Significant at 0.01, 0.05**
Significant at 0.05*

There was a correlation between IL-4 and IgG1 ($r = 0.77$, $p < 0.01$) that confirms Th2-promotes the production of IgG1 this agrees with Severinson [30].In addition to presence of correlation between IL-10 and IgG1 ($r = 0.86$, $p < 0.01$) that links regulatory cytokines to IgG1 class-switching as this regulatory cytokine link to the B-cell class-switching process that results in IgG1 production. Moderate Correlations was showed between IFN-γ positively correlated with all IgG subclasses, suggesting cross-talk between cellular (Th1 and B cells) and humoral immunity. The wide correlation of IFN-γ with all IgG subclasses focus on its dual role, it can stimulate protective immune responses while also possibly contributing to pathological ones.IL-4 and IL-10 are essential to IgG1 production, highlighting their role in B-cell stimulation [31][32].

4. CONCLUSIONS

The study showed that interleukins (IL-4, IL-10, and IL-17) contribute to the activation of the Th1 cellular immune response, which is crucial for eliminating cutaneous leishmaniasis. Elevated levels of interferon-gamma (INF-γ) in clinically improved patients may indicate its essential role in stimulating phagocytic cells to eliminate intracellular parasites. Furthermore, the observed increase in certain IgG immunoglobulins (IgG1, IgG2, IgG3, and IgG4) suggests the role of these immunoglobulins in the immune response to cutaneous leishmaniasis.

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