

Immunomodulatory Impact of Th1 and Th2 Cytokine in Human Scabies

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Abstract

Scabies disease is parasitic infection and skin invasion caused by genus of arthropod called a mite recognized as *Sarcoptes scabiei*, they proliferate on the skin surface by drilling and laying eggs if it untreated and can alive for many months. This study will discuss the function of inflammatory cytokines in relevance to disease exacerbation in scabies patients and role between immune responses of established on Th1 (pro-inflammatory cytokines) and Th2 (anti-inflammatory cytokines) parameters by measured interleukins IFN- γ and IL-13 respectively. Both cytokines significantly increased in the level of probability ($P \leq 0.01$) of the sera of scabies patients compared to control people. Result showed Interferon gamma (IFN- γ), (is the major mediator of cellular immune responses, which excrete from Th1 that stimulate parasite control by improve the capacity of macrophage cell to killing intracellular parasite), level concentration has increased in patients group (186.49 pg/ml), whereas decreased compared with healthy people results was (150.42 pg/ml). Regarding, the immune interleukin (IL-13) level, where it reached concentration (458.12 pg/ml), while results decreased in control group was (371.60 pg/ml). This interleukin (IL-13), which protection human from against parasite illness and in addition to increase of proliferation of immunoglobulin's specially IgE that important role in hypersensitivity infection include scabies disease, which was reflected his function in increasing concentration in scabies patients. Moreover, it was found that there is an increase in the secretion of IL-13 in addition to elevate IFN- γ level in the patient's serum, because scabies disease stimulated to both Th1 and Th2 immune responses. However, these current results indicated that the immune responses in scabies disease anti-inflammatory more than pro-inflammatory. Finally, equiponderant immune responses and cytokines connection appear to play about a pivotal role through scabies disease.

Keywords: *Sarcoptes scabiei* , IL-13 , IFN-gamma, Th2 cytokines, Th1 immune response.

1. Introduction

Scabies is a parasitic sickness caused by infection of skin through the burrowing mite *Sarcoptes scabiei*, scabies is a main health issue and prevalent in developing countries and different regions of worldwide assuming more than 100 million person (19). Scabies affects all ages (although, some countries of Latin American and Pacific regions have a high onus of scabies and spread is basically in children than in youth and adults) (22), any gender as well in all ethnic groups and socioeconomic level (18).

This disease is transmitted via skin-to-skin connect (9). The major illness appearance are intermediate by flaming and hypersensitivity-like reactivity to mite products leading to different pruritic lesions (14), therefore patients with scabies suffer from heavy itching arrange through allergic and inflammation reactions caused by the host versus the parasite (mite) and their products. (19).

The clinical manifestations of scabies have been reported to be extensive from mild to severely destructive (8). In addition to this immediate burden, scabies is also related to secondary complication such as acute post-streptococcal glomerulonephritis (APSGN) and rheumatic heart disease (RHD) and this side effects, if left untreated, can lead to development of serious, life-threatening downstream

conditions (12). Spontaneous recuperation of scabies in humans has been described as only occurring with sequent re-infestation (24). In spite of the health and economic importance of Sarcoptic infection in both human and animal inhabitation, pathogenesis and immune reaction of this disease are not yet well understood and still poorly described (14).

Interferon gamma (IFN- γ) is mostly produced by activating T cells and natural killer cells (NKc), and can elevate phagocyte activation, intermediate antibacterial and antiviral immune (10). Promote antigen presentation cell (APC) of the innate immune system, assortment endothelium-lymphocyte interaction (21).

Interleukin 13 (IL-13) is a 12-kDa cytokine biological activity on macrophage/monocyte, endothelial and B cells, IL-13 is firstly generated by Th2 cells, but it is also produced by another T helper cell subset mast cells, CD8+ T cells, basophile, and eosinophils (7).

2. Materials and Method

The present study inclusive fifty patients sufferance from scabies disease in multiple parts of the body, by consultant specialist of the dermatology department in Abo - Gahrib Public Hospital, Ameriya general polyclinic and Tikrit teaching hospital during the duration from the 1st December 2019 to October 2020.

The patients were examined to comparison of immune response between them and healthy people were blood

samples collected from this group included fifty two individuals as a control group. Diagnosis of scabies disease easy by clinical as well as path gnomonic signs, which confirms this description of infection for scabies patients.

Blood collection, for each entrant, (7ml) venous blood specimen is withdrawn, placing in a plain test tube, and left to stand for 35 minutes at room temperature for coagulate formation for serum collecting, the tubes were centrifuged at (2500 rpm) for (15 minutes), for serum experiment by Eliza mechanism and ELISA Kit provided is model, serum was aspirated using a Pasteur pipette and distribute at sterile Eppendorf tubing and stocked at (-20C°) until used.

Assay Procedure of Human IFN-gamma ELISA Kit

According to the manufacturers instruction (Koma Biotech, Korea), No. K0331121, of IFN- gamma based on sandwich ELISA format (enzyme-linked immune-sorbent assay) technology.

Assay Procedure of Human IL-13 ELISA Kit

According of manufacturers instruction (Koma

Biotech, Korea), No. K0331235, by a solid phase sandwich ELISA format technique.

Statistical Analysis

Statistical Analysis System- SAS (2018) program was applied to impact various factors in study parameters. Least significant difference –LSD test (ANOVA) t-Test was used to significantly compare between methods.

3. Result and discussion

The approaching study included a hundred personnel, which divided into two major groups: fifty healthy individuals as a control with the same number of scabies disease patients.

Serum Level of Th1 cytokines

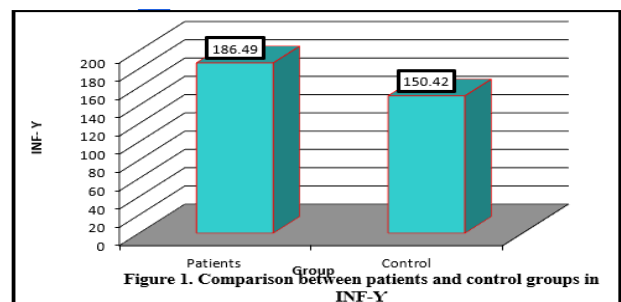
Interferon gamma (IFN-γ)

Increasing value of IFN-γ (Th1) in serum of patient group with scabies disease (186.49 pg/ml) , so, showed high significant in the level of probability(P≤0.01) compared with healthy people (control group) results was (150.42 pg/ml) (table 1).

Concentration of (IFN-γ) (pg/ml) (Mean ± SE)		
Group	No.	Mean ± SE of IFN-γ
Patients	50	186.49 ± 8.72
Control	50	150.42 ± 5.49
T-test	---	20.462 **
P-value	---	0.00078

** (P≤0.01).

Eosinophil submit may themselves modify or tolerate local Th2 inflammatory response, in scabies disease, eosinophils suggest else organize Th1 inflammatory responses, since it produce IFN-γ (6). Therefore, results showed increases in IFN-γ level in patients from healthy people. This result agreement with (16). Since IFN-γ is from proinflammatory cytokines and inhibition by Th2 cytokine lead to tardiness in symptom in disease onset only (11) (2). Thus, IFN-γ has substantial function in innate defense versus parasite as the raised impedance to scabies infection (19). Mostly, hypersensitivity is comprehend to be unbalanced among the Th2 and Th1 immune reactions, thus, (IFN-γ) cytokine have been insitute to increase the inflammatory operation and not to ameliorate allergic immune responses (5) (Fig. -1).



Serum Level of Th2 cytokines

Interleukin IL -13

Present results showed high significant increasing level of IL-13 (Th₂) in serum of patient groups with scabies disease (458.12 pg/ml), in the level of probability(P≤0.01), while results decreased in control group was (371.60 pg/ml) (table 2).

Concentration of IL-13 (pg/ml) (Mean ± SE)		
Group	No.	Mean ± SE of IL-13
Patients	50	458.12 ± 18.57
Control	50	371.60 ± 15.55
T-test	---	48.075 **
P-value	---	0.0006

** (P≤0.01).

Interleukin 13 is cytokine answerable for Th2 response in human. progressive from T cell in addition to eosinophil (has a role in deterioration in allergic illness) and mast cell, therefore IL-13 is

usually associated with allergic inflammations, inclusive asthma and scabies, since, IL-13 organize the function of humans B cell (IgE) and monocyte (is a kind of W.B.C . it the large type of leukocyte and can distinguish into dendritic cells (Dc)), thus it a

sharing in innate immune system as well effect on adaptive immunity of vertebrate (3). Therefore, it causes IG isotype transition in B lymphocyte into IgE, and the last, have role in evolution of allergic (20), therefore IL-13 is as vigorous of fibrosis in many inflammations and autoimmune disease, which lead to an increase in the value of interleukin in patients suffering from scabies disease, and this study corresponds to (13)(4) (Fig. -2).

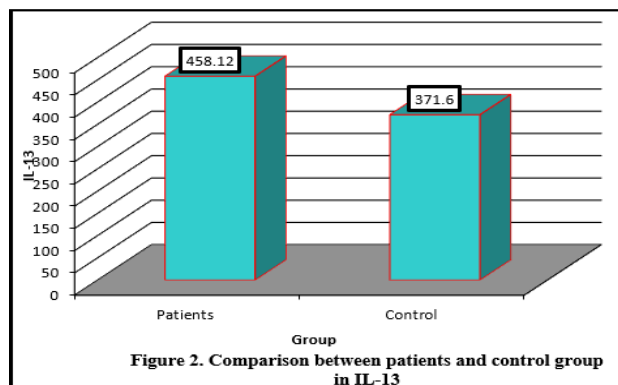
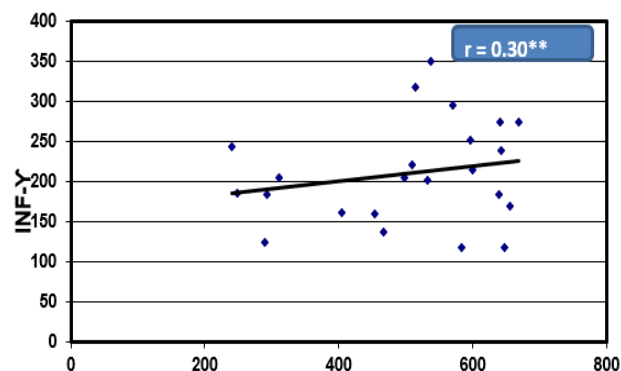


Figure 2. Comparison between patients and control group in IL-13
Correlation between the concentrations of immunological cytokines (IL-13 and IFN- γ) of scabies patients specimens

Immune responses in patients with scabies were stimulated by increased levels of Th1 and Th2 cytokines at varying times (IL-13 and IFN- γ) (Fig. -3).



Since it is scabies disease induced two very excrete Th1 as (IFN- γ) and Th2 (IL-13) cytokine excretion types, this may due to, IL-13 and IFN- γ play professional role in alternative macrophage activation (Macrophages correlating with pro-inflammatory, allergic disease and parasite contagion) and these cytokines have been recorded in immune responses to scabies illness (24)(15). This study is consistent (23) which showed macrophages although in low numbers, have been detected in skin of patients with scabies.

Although IL-13 is secreted in high quantities, the severity and symptoms of the disease are not reduction, this may be due to little number of macrophages may do for produce of immune modulate molecule excrete by the scabies mite (1). It lead to may be that precocious infection mites prevent efficiency of this cells to emigrate to position of inflammation, allow the mite to increase and reside (18). In addition to rising level of IFN- γ especially in onset of the disease, and with the appearance of symptoms and the worsening of the

patient's condition, it begins to be inhibited by an increase in the secretion of IL-13. It is worth mentioning, in scabies disease, both immune responses of (Th1 and Th2), continue extremely expressing, but, so far is not comprehended why scabies illness can induce peak values of both Th1 and Th2 cytokines since they commonly down-regulate each other, however, this Th2 tilt responses may do a cause of instead of a response to scabies mite (19).

This fisticuffs of immune responses for pro-inflammatory and anti-inflammatory cytokines and macrophages in scabies poverty more realization into their study, function and role in immune and inflammatory response in scabies mite disease.

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