Evaluation of the Immune Response in Scabies Patient (Ordinary and Prisoners) Treated with Permethrin 5%

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Abstract

Scabies is a common parasitic infection, caused by sarco-sarcoptes, the infection occurs when the *Sarcoptes* penetrates the corneal layer of the skin, predominant pathological manifestations, through inflammatory and allergic reactions to mite products.This study is designed to obtain the Evaluation of the immune response in scabies patient (Ordinary and Prisoners) treated with Permethrin 5%.The study included (28)Ordinary Scabies patients, (32) prisonersas well as a (30)healthy person as a control group. Blood samples were collected from all studied groups Enzyme-linked immunosorbent assay (ELISA) was used to measure Interleukine-4,IL-9 and total IgE.Results of the study showed that serum,IL-4 showed a significant ($P \leq 0.0001$) increasing in prisoners compared to ordinary patients and control groups(248.8±19.3vs.79.2±10.7pg/ml),(248.8±19.3vs.73.9±5.5pg/ml)respectively,while IL-9 showed a significant ($P \leq 0.001$), increasing in control compared to Ordinary Scabies patients group and prisoners (506.9±48.7vs.337.8±18.2 pg/ml), (506.9±48.7 vs. 424.1±36.5 pg/ml) respectively in post- treatment, There was positive correlation between (IL-4 and IgE).Levels of two cytokines (IL-4, and IL-9) were assessed in sera of Ordinary ScabiesPatients and control group, IL-4 showed a significant ($P \leq 0.0001$) increasing in Ordinary Scabies comparedto control group (92.5±7.0 vs. 73.9 ± 5.5pg/ml), respectively. While IL-9with asignificant decreasinglevel inOrdinary Scabies patients compared to control group(97.8 ±18.8 vs. 506.9 ±48.7 pg/ml) in pre-treatment, level of IgE were recorded in pre- treatment in ordinary patients and prisoners (314.8±37.5 vs. 17.8±3.7 IU/ml), (372.7±37.5 vs. 17.8±3.7 IU/ml) respectively, were a significantly increasing ($P => 0.05$) as compared to healthy control. In post- treatment IgE levels show a significantly lowering ($P => 0.05$), in prisoners than Ordinary patients(14.5±1.7 vs. 33.3±2.4 IU/ml).

Keywords: *Scabies,IL-4, IL-9, totalIgE.*

Introduction

Scabies is one of the diseases that are considered an endemic and epidemic in Iraq, it's a common parasitic infestation of global proportion, the source of scabies, prisons, military, relatives and hospital admission and travel, it's also affects many wild animals, causing severe economic losses**(1).** Although *Sarcoptes scabiei* worldwide spreads easily through close physical contact, Scabies is an acute itching disorder caused by an immune response to skin allergies and inflammatory reaction, IL-4 and IL-13, supporting their contribution to allergic inflammation, cause to increase IgE production, the elevated level of IL-4 suggests a preferential activation of TH2 cells and regulates IgE production, In addition to persist symptoms after treatment, most male prisoners are specifically of the type of nodular scabies **(2).**Increased physiological stress can have profound effects on the immune system**(3).**The effects of Glucocorticoid are the suppression of immune response mediators **(4).**Glucocorticoid secretion is increasingly used as an endocrine indicator **(5)**. Nervous tension plays a key role in the mechanism of response by the release of glucocorticoid **(6).**This study was conducted

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to evaluate the immune response in IL-4, IL-9and total IgE, in Ordinary scabies patients and Prisoners treated with Permethrin 5%.

Immune response against scabies disease:

Scabies mites are believed to have developed the ability to modify different aspects of the host's immune responses **(7).**

Prevent early immune and anti-inflammatory reactions, this delay allows to secrete unknown antigens that stimulate the proliferation of Regulatory cells and their secretion of IL-10, which would inhibit the inflammatory and immune responses in humans to the mites before a strong immune response occurs, resulting in delayed onset of symptoms**(8).**

Role of IL-4

Interleukin-4 is a multifunctional cytokine that plays an important role in regulating immune responses**(9).** Its effects depend on correlation and signaling through a receptor complex consisting of the IL-4Rα series and the common gamma chain (γc), leading to a series of phosphorylation events with kinases associated with receptors. This shift leads to the recruitment of mediators for cell growth, apoptosis resistance, gene activation and differentiation**(10).**

Role of IL-9

Initially, T cells were the main source of IL-9 since their discovery in 1988 were linked to the Th2 phenotype due to the location of genes within the Th2 cell and their preferential secretion with other cytokines, NKT cells are produced IL-9 that have been processing for nasal lymphoma cell lines (11).IL-9 has multiple cellular sources that may affect its polymorphic functions (pleiotropic) cytokines were studied primarily in the context of immune pathogenic T-helper-2.

IgE

IgE is important in defending the host against a variety of parasites, along with mast cells, basal cells, eosinophil, is an essential component of allergic inflammation and parasites. In humans, previous studies have shown that scabies lead to increased antibody production of IgE but with very different results **(12).** In allergies, activation of mast cells mediated by IgE depends on the antigen dose and route of entry, in the early stage increase in *S. scabiei*numbers subsequent to primary infestation with elevation of IgE, and then gradual reduction as host immunity develops; **(13). (14); (15);(16).**

Material and Methods

Subjects:

Blood samples were collected from two groups: First- inmates including: Juvenile Prison and Iraqi Reform Section, (32 prisoners) aged (15-63 years), Second group: Ordinary Scabies patients in Allergy and Consultative Asthma Center (28 person), the ages ranged from (8 - 67) years, with (30 health person) as control group.The disease was diagnosed by a dermatologist; prisoners are sampled with the consent of the prisoner through a signature and thumbprint without any pressure.All samples were collected at period from May to August 2019.

Blood sample collection

Under sterile conditions, 2 ml of peripheral blood was withdrawn from patients and distinctly healthy control, and three were separated in a gel tube for 30 to 60 minutes for automatic coagulation at room temperature before centrifugation at 3000 rpm for 10 minutes, The obtained serum was divided into 3 Eppendorf tubes, and stored in Frozen at -20 ° C for serological tests. Elisa technique was performed to estimated serum level of IL-4,IL-9 and total IgE of all studied groups.

Clinical examination

The clinical examination had been done by the dermatologists in hospital and the scabies diseases were diagnosed according to clinical features.

Statistical Analysis:

Results are expressed as mean ± standard errors (M±SE) which were analyzed by one-way analysis of variance (ANOVA) followed by Fisher's test for multiple comparisons, using Stat view version 5.0. Differences were considered significant when $p<0.05$. The other data expressed as percentage (%) which were analyzed by chi square test using excel program version 2010. Regression analysis was performed by analysis of covariance (ANOVA) also using Stat view version 5.0.

Results

Results of Immunological study

Total serum level for IL- 4, IL-9 and total IgE were investigated in serum of (ordinary Scabies patient and Prisoners as well as healthy control) groups. Results of the current study showed that serum Levels of two cytokines (IL-4 IL-9). were assessed in sera of scabies patients and control, IL-4 showed a significant ($P \leq 0.0001$) increasing in prisoners compared to ordinary patients groups(248.8±19.3vs.79.2±10.7pg/ml),(248.8±19.3vs.73.9±5.5pg/ml) respectively, while IL-9 showed a significant ($P \leq 0.001$), increasing in control compared to Ordinary Scabies patients group and prisoners (506.9±48.7vs.337.8±18.2 pg/ml), (506.9±48.7 vs. 424.1±36.5 pg/ml) respectively in post-treatment, There was positive correlation between (IL-4 and IgE). Levels of three cytokines (IL-4 and IL-9) were assessed in sera of Ordinary Scabies Patients and control group, IL-4 showed a significant ($P \leq 0.0001$) increasing in Ordinary Scabies compared to control group (92.5±7.0 vs. 73.9 ± 5.5pg/ml). While IL-9 with a significant decreasing level in Ordinary Scabies patients compared to control group (97.8 ±18.8 vs. 506.9 ±48.7 pg/ml) in pre-treatment, as shown in Table (1).

Table (1): Comparison of serum level of IL-4,and IL-9Ordinary Scabies patients and prisoners as well as control according to treatment.

Groups	IL-4 (pg/ml)				IL-9 (pg/ml)	
	Mean±S.E.				Mean±S.E.	
	Post-treated	Pre-treated			Post-treated	Pre-treated
Control		73.9±5.5				506.9±48.7*
Ordinary	79.2±10.7	92.5±7.0*			337.8±18.2	97.8±18.8
Prisoners	248.8±19.3*				424.1±36.5*	
P. value	<0.0001	0.049			0.043	0.003

*** Different letters= Significant difference (P≤0.05) between mean.**

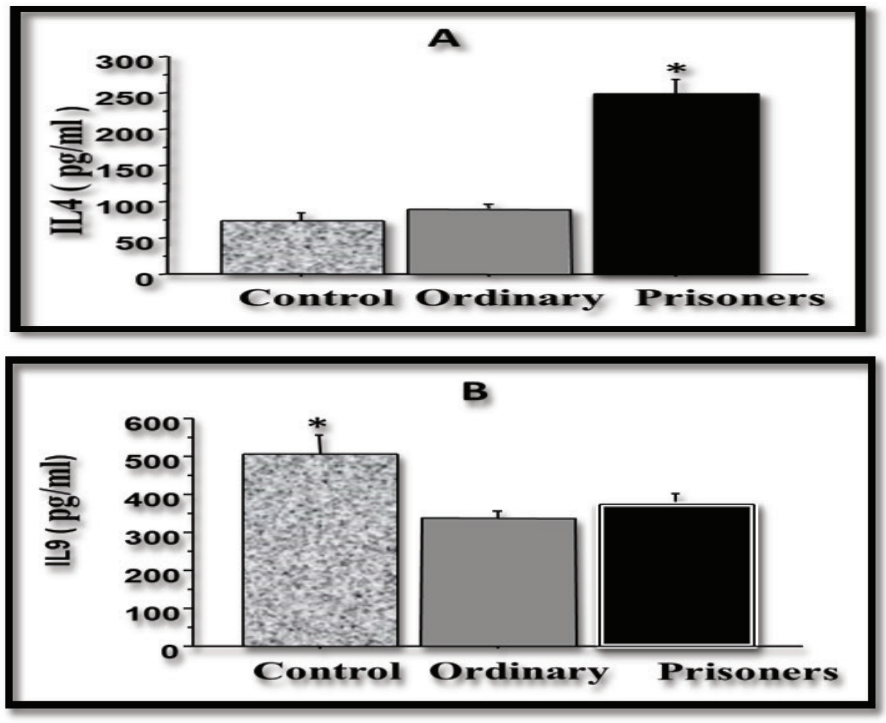

Figure (1):Comparison of serum level of IL-4 and IL-9 in scabies patients and prisoners as well as control according to treatment.

Level of IgE were recorded in pre-treated in ordinary patients and prisoners (314.8±37.5 vs. 17.8±3.7 IU/ml), (372.7±37.5vs.17.8±3.7 IU/ml), respectively were increased significantly (P <0.05) as compared to healthy control. In post- treatment serum IgE levels show a significantly lowering(P <0.05), in Prisoners than ordinary patients (14.5±1.7 vs. 33.3±2.4 IU/ml) the total serum IgE in ordinary patients and prisoners as shown in table below (2).

Table (2): Comparison of total IgE levels pre- and post-treatment in ordinary scabies patient and prisoners as well as healthy control groups.

Groups	IgE (IU/ml) pre-treatment	IgE (IU/ml) post-treatment	P.value
Control	17.8±3.7		
Ordinary	314.8±37.5	33.3±2.4*	<0.0001
Prisoners	372.7±37.5	14.5±1.7	<0.0001
P. value		C. vs O.	<0.0001
	C. vs P. <0.0001		
	P. vs O. NS		
	P. vs O.=0.002		

*ANOVA test was used to compare between ordinary patients groups with control group and prisoners group with control (H.S.: Highly significant).

* N.S: Non-Significant.

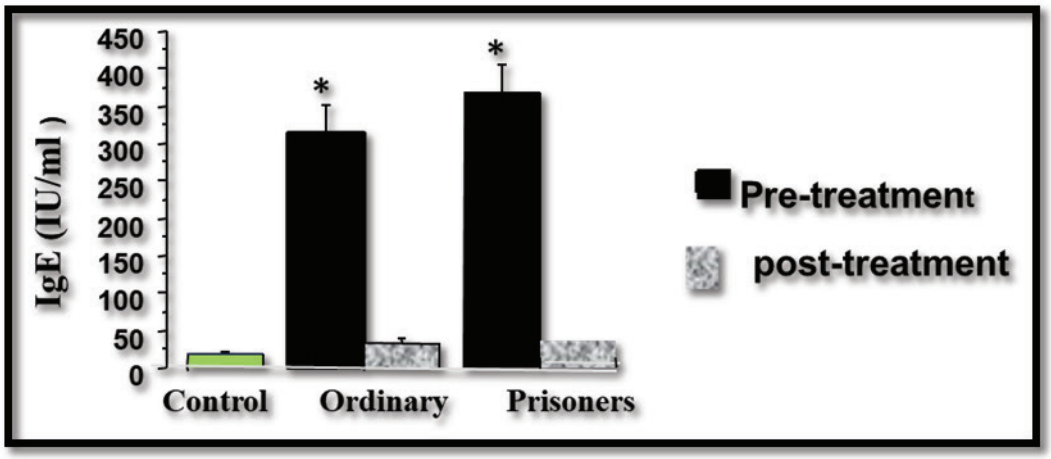

Figure (2): Comparison of IgE level of ordinary scabies patients and prisoners as well as control according to treatment.

Correlation between IgE and cytokines

Data from this study found that IgE positively correlation was observed between IL-4 and IgE, while IL-9 had a negative correlated with IgE, in the pre-treatment. A negative correlation between IL-4, IL9 and IgE in post-treatment, as shown in table (3).

Table (3): Correlation coefficient between IgE and cytokines according to treatment.

IgE	**IL-4**		**IL-9**
Post-treatment	R=0.16 P.value=0.254		R=0.14 P.value=0.189
Pre-treatment	R=+0.44 P.value=<0.0001		R=0.73 P.value=0.85

-Correlation coefficient®

Discussion

The scabies test depends on the duration of infestation at the time of the test and the length of treatment, Th2 cells are important for the production of major cytokines, including IL4 and IL5, these cytokines are important role for class switching antibody, regulating systemic IgE synthesis, IgE level in Ordinary scabies and prisoners was Significantly increasing compared to controls, in pre- treatment (P=>0.0001), in post-treatment IgE levels show a significantly lowering in Prisoners than Ordinary patients **(17),**IL-4 showed a significant ($P\leq$0. 0001) increasing in prisoners compared to ordinary patients and control groups, while IL-9 showed a significant ($P\leq$ 0.001), increasing in control compared to Ordinary Scabies patients group and prisoners, in post-treatment, There was positive correlation between (IL-4 and IgE). Levels of three cytokines (IL-4 and IL-9) were assessed in sera of Ordinary Patients and control group, IL-4 showed a significant ($P\leq$0. 0001) increasing in Ordinary Scabies compared to control group. While IL-9 with a significant decreasing level in Ordinary patients compared to control group in pre-treatment. Prison was the main source of scabies infestation (80%). this may be due to overcrowding, poor hygienic standards; sharing the beds and prolonged contact with contagious infested prisoners, similar results were observed in previous Iraqi studies **(18); (15)** which reported that prisoners were responsible for infesting 83.3% and 60% of the Ordinary scabietic patients.From these studies, there appear to be differences between immune responses to humans.These responses may also be affected by due to duration of infestation and type of infestation in humans and host gender.The current results in agreement with **(19),(20**). Demonstrated a statistically significant elevation of IL-4 in scabietic patients (Ordinary and prisoners) as compared in controls.In our study, the results were different for ordinary patients and prisoners because most prisoners were under treatmentthe theory may vary in prisons in terms of morbidity, personal and social behavior, treatment, the nature of nutrition and the closed and densely populated environment and contact with others, The category covered is prisoners may carry diseases that may lead to the development of immunity and events in complications of the disease with common diseases, including psoriasis and autoimmune… ect **(21);(22).**Most prisoners with permanent symptoms with re-infestation due to Failure to take appropriate administration to prevent the disease and use the treatment incorrectly, while others suffer from simultaneous conditions with scabies, such as chronic or acute infections, Some male prisoners specifically have a nodular scabies type, and this type may take another route in terms of treatment and persistent symptoms after treatment nodules can last for several weeks or months after treatment and may require corticosteroid injections**(2**). Topical treatments are effective, but the most effective ones, permethrin 5%, alternative therapies may be less effective, poorly tolerated, or have more significant adverse effects such as sulfur, benzyl benzoate;The data showed that interleukin-9 is not induced by scabies proteins.In allergies, activation of mast cells mediated by IgE depends on the antigen dose and route of entry, in the early stage increase in *S. scabiei* numbers subsequent to primary infestation with elevation of IgE, and then gradual reduction as host immunity develops; This findings agreed with other studied (**14); (15); (16**).In our study we observed there is one explanation in the action of permethrin to reduce inflammation and eliminate allergic reactions in the

immune aspect: The most common anti-scabies treatment (permethrin 5%) inhibits activity and production of T cells, which are predominant cells in the inflammatory process by blocking the signal pathway, preventing the release of histamine from mast cells and basal cells**(23).** Antihistamines block histamine signaling pathways and thus will prevent cell migration to inflamed tissues and thus reduce the production of inflammatory mediators and cytokines.

Conclusion

Interleukin-9 has a non-specific effect on local allergies and is not induced by scabies proteins, while it has an effect on systemic allergies.

Acknowledgment: We are thankful to the all patients for providing all samples in this study. All samples were collected after taking security statements from the Minister of Justice, the Iraqi Juvenile Reform Administration and the Baghdad Health Department in Karkh, samples of prisoners are taken with the consent of the prisoner by pledge, signature and thumbprint without any pressure.

Conflict of Interest : None

Source of Funding : Self

Ethical Clearance : From patients and my college .

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