The indirect induction of human scabies to initiation autoimmune disease (SLE): Comprehensive study in marshes population of Thie-Qar

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Key words: scabies-SLE, antioxidant activity, scabies

Abstract

Scabies is one of the disease that is considered an endemic and epidemic in Iraq, in this study it has been observed that other disease were found to be associated with scabies patients, and in order to investigate the mechanism by which the scabies may induce other disease (such as SLE) an immunological, hematological and immunobiochemical tests were investigated both in patients having scabies and scabies-SLE disease. High sensitive C-reactive protein was higher significant in all groups compared with control and higher significant in scabies-SLE as compare with scabies patients, IgG was higher significant in all groups as compare with control, lower significant in scabies-SLE as compare with scabies patients. IgM was higher significant in scabies patients as compare with control and lower significant in scabies-SLE. IgA was higher significant in all groups as compare with control. IgE was higher significant in all groups as compare with control, but lower significant in scabies-SLE as compare with scabies patients. C3 and C4 was lower significant in scabies-SLE as compare with both control and scabies patients. IL-6, IFN-γ, IL-18 and TNF-α was higher significant in all groups as compare with control also higher significant in scabies-SLE as compare with control. IL-1β was higher significant in all groups as compare with control, but not as compare scabies patients. IL-5 was higher significant in scabies as compare with control, but lower significant in scabies-SLE as compare with scabies. Eosinophil and neutrophil were higher significant in scabies as compare with control. Eosinophil, neutrophil, basophil and monocyte have lower significant in scabies-SLE as compare with control and scabies patients. superoxide dismutase (SOD) activity was higher significant in scabies patient only as compare with control, but lower significant in in scabies-SLE as compare with both control and scabies patients. Malondialdehyde (MAD) level was higher significant in scabies-SLE as compare with control. All data were considered significant at ($P<0.05$). The mechanisms of inflammation induced by mites may be related to the generation of excessive level of cytokines and antibodies against its proteins, so that triggering of excessive inflammatory responses, then developing autoimmune disease likes SLE.

الحث الغير مباشر لمرض الجرب لنشوء مرض المناعة الذاتية (الذؤابة الحمراء): دراسة شاملة على سكان الاهوار في محافظة ذي قار

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الكلمات المفتاحية: الجرب, الجرب والذؤابة الحمراء, فعالية مضادات الاكسدة

الخلاصة

يعتبر مرض الجرب في العراق من الامراض الوبائية المتوطنة, تم ملاحضة الاصابة بأمراض اخرى بالاضافة الى مرض الجرب, لمعرفة الميكانيكية المناعية التي من خلالها يحث الجرب على ظهور امراض اخرى, تم اجراء بعض الفحوصات المناعية و البايوكيميائية وبعض فحوصات الدم, اظهرت النتائج ات هناك ارتفاع معنوي لكل من(hs-CRP, IgG, IgE, IgA) في كل مجاميع الدراسة مقارنة بمجموعة السيطرة, وارتفاع معنوي في مستوى (IgM) في مجموعة مرضى الجرب مقارنة بمجموعة السيطرة, كان كل من IL-1β, IL-18, IL-6) IFN-γ, TNF-α) مرتفع معنويا في كل المجاميع مقارنة بمجموعة السيطرة, كانت (Eosinophil and neutrophil) مرتفعة معنويا في مرضى الجرب مقارنة بالسيطرة, كانت فعالية (SOD) مرتفعة معنويا في مرضى الجرب مقارنة بالسيطرة, اظهر (MAD) ارتفاع معنوي في مرضى الذؤابة الحمراء مقارنة بالسيطرة. نستنتج من هذه الدراسة ان بروتينات طفيلي الجرب تثير تفاعلات التهابية مناعية مفرطة , تحفز ظهور امراض اخرى.

Introduction

Scabies is the most common parasitic infestation, in the Worldwide its estimated almost three hindered million cases occur annually [1]. The "arthropod Sarcoptes scabiei var hominis" causes contagious skin infestation and heavy pruritic which affects human of all socioeconomic status [2]. more than 2500 years Scabies infestation has been reported, Aristotle discussed the "lice in the flesh," then Celesus recommended to using sulfur mixed and liquid pitch as a drug for the disease [3]. in 1687 scabies was ascribed to the mite by Giovan Cosimo Bonomo. Scabies was the first human disease which caused by a specific pathogen [4]. Approximately hundreds to millions of mites can infest the host, that usually child, elderly and immunocompromised [5]. severe dermatitis or psoriasis can be confused with Crusted scabies, so crusted lesions appear as a thick and hyperkeratotic scales over the knees, palms, elbows, and soles, when suspected dermatitis or suspected psoriasis, do not respond to treatments then the diagnosis of crusted scabies can be considered [6]. Usually Serum immunoglobulin E, IgG, and neutrophil are higher in scabies patients, but the immune reaction does not seem to be protective [7]. In scabies CD4 T-cell infiltrate in the skin, as a Cell-mediated immunity [8]. After a long persistency of scabies parasites in the host, a specific immune response will occur, with activation of Th-2 cells, leading to increasing in eosinophilia and interleukin-5 [9]. intra-epidermal often suprabasal blisters, can develop by the Secretion of proteolytic enzymes near the basal membrane zone, in a patient with a positive result for biopsy and immunofluorescence, the scabies mites may triggered a signal for development autoimmune disease [10].

Material and methods

This study done in the population of marshes in thie-Qar governorate, were they suffer from spread of scabies, particularly in their children. The patients didn't use any treatment because of the poor living conditions, so they were proper cases for study. 34 scabies patients were included in our study from July 2012 to July 2016, they were divided into two groups: (22 scabies patients: male:9 and female:13) and (12 scabies-SLE: female 12), also 20 cases control were included. All patients were diagnosed by mites testing IgG antibodies against "*Sarcoptes scabiei* in serum (ELISA,AfosaGmbH, Dahlewitz/Berlin,Germany)", all cases were serologically positive for anti-*Sarcoptes* IgG. The questioner formats also doing for each group: age; gender; time of onset of scabies, other information were recorded. Immunological, hematological and immunobiochemical tests were done. by using venous blood. high-sensitivity C-reactive protein in plasma detected by"Turbidimetric Kit with specific high-sensitivity methodology (BioTécnica, Brazil)", serum complement components C3 and C4, serum IgA, IgG and IgM were measured using radial immunodiffusion (RID Kit, LTAonline, Italy). While "IgE level was measured by using enzyme-linked immunosorbent assay (IgE ELISA Test Kit, Genzyme, CA, USA)". Serum TNF-α, IL-6, IL-10, IL-5, IL-1β, and IL-18 levels were determined using ELISA kits (R&D Systems, Shanghai, China). Differential count was performed by using "CYAN Hemato analyzer automatic hematology analyzer", (Catalog No.CY006.Diagnostic, Langdorpseteenweg160, B-3201Belgium). Also The oxidative stress parameters were analyzed, MDA level in serum was determined as per method described by Satoh [12], activity of SOD was determined, the "percent inhibition of the formation of NBT-diformazan by SOD is represented by the activity of SOD as describe by (Liocher & Fridovich, 2007)".

Statistical analysis

Data are described as the mean±SD, SPSS17 program was used for statistical analysis, Statistical significance was at (P<0.05), so that data was considered statically significant when p-values were less than 0.05.

Result

According to the age, scabies patients were divided into four age groups, the highest ratio for scabies patients incidence was in children (7-15). The highest ratio for scabies-SLE patients incidence was in adult (16-25), as shown in table (1). According to the gender, the highest ratio of female was in scabies patients and it similar in scabies-SLE group. Table (2) illustrate gender distribution in this study.

Table (1): Age distribution of scabies in all groups

Age (years)	Scabies n=22	Scabies-SLE n= 12
7-15	12	0
16-25	5	10
26-39	3	2
40-52	2	0

Table (2): Gender distribution in all groups

Scabies n=22		Scabies-SLE n= 12	
Male	female	Male	female
9	13	0	12

Result in table (3) shown that the level of hs-CRP was higher significant in all tow groups (4.29±0.4 and 7.65±0.2) as compare with control, also have higher significant in scabies-SLE as compare with scabies patients at ($P < 0.05$). IgG was higher significant in all groups (1653.81±98.1 and 1141.3±31.4) as compare with control, lower significant in scabies-SLE as compare with scabies patients. IgM was higher significant in scabies patients (210.8± 14.3) as compare with control and lower significant in scabies-SLE (113.2± 2.6) as compare with control. IgA was higher significant in both groups (218.8±20.4 and 219±2.36) as compare with control. IgE was higher significant in both groups (0.053±0.02, and 0.031±0.04) as compare with control, but lower significant in scabies-SLE as compare with scabies patients. C3 and C4 was lower significant in scabies-SLE as compare with both control and scabies patients. IL-6, IFN-γ, IL-18 and TNF-α was higher significant in all groups (59.98±34.1, 61.39±3.6,:56.1±16,62.2±2.4,:104.93±3.48,112.34±2.5,:326±22,330) respectively as compare with control also higher significant in scabies-SLE as compare with control. IL-1β was higher significant in both groups (29.94±1.12, 30.42±3.2) as compare with control, but not as compare scabies patients. IL-5 was higher significant in scabies (6.4±1.4) as compare with control, but lower significant in scabies-SLE (3.6±4.2**)** as compare with scabies.

Table (3): level of immunological parameters in all groups

Parameters	Control n=20	Scabies n=22	Scabies-SLE n=12
hs-CRP(mg/L)	2.11±0.4	4.29 ± 0.4	7.65±0.2
C3 (mg/dL)	99.28±25.1	100.3±81.3	89±20
C4 (mg/dL)	26.62±5.61	27.4±18.2	21.3±15.2
IgG (mg/dL)	1130.50±67.2	1653.81±98.1	1141.3±31.4
IgM (mg/dL	140.1±76.8	210.8± 14.3	113 .2± 2.6
IgA (mg/dL)	129.9±12.7	218.8± 20.4	219± 2. 36
IgE (mg/dL)	0.018±0.02	0.053± 0.02	0.031±0.04

TNF-α (pg/ml)	**22.84± 6.34**	**326 ±22**	**330±14**
IFN-γ (pg/ml)	**13.0±4.2**	**56.1±16**	**62.2±2.4**
IL-6 (pg/ml)	**3.58 1.34**	**59.98±34.1**	**61.39±3.6**
IL-1β (pg/ml)	**8.9±5.2**	**29.94±1.12**	**30.42±3.2**
IL-18 (pg/ml)	**45.6±2.5**	**104.93±3.48**	**112.34±2.5**
IL-10 (pg/ml)	**0.82±0.56**	**1.03±1.2**	**2.01±3.2**
IL-5 (pg/ml)	**3.2±2.4**	**6.4±1.4**	**3.6±4.2**

The result describe as Mean±SD, significant at (P <0.05)

Table (4) illustrate the significant and no significant value for all immunological parameters, so that when compare between control and scabies groups all parameters were significant except C3 and C4.whene compare between control and scabies-SLE only IL-5 were non-significant, while C3, C4 and IgM were lower significant. When compare scabies with scabies-SLE the IgA, IL-1β were non-significant, also IgM, IgG, IgE and IL-5 were lower significant.

Table (4): Significant and no significant value for immunological parameters.

Parameters	C vs. S	C vs. S-SLE	S vs. S-SLE
hs-CRP(mg/L)	**S**	**S**	**S**
C3(mg/dL)	**NS**	**S** Lower	**S** Lower
C4(mg/dL)	**NS**	**S** Lower	**S** Lower
IgG(mg/dL)	**S**	**S**	**S** Lower
IgM(mg/dL	**S**	**S** Lower	**S** Lower
IgA(mg/dL)	**S**	**S**	**NS**
IgE (mg/dL)	**S**	**S**	**S** Lower
TNF-α (pg/ml)	**S**	**S**	**S**
IFN-γ (pg/ml)	**S**	**S**	**S**
IL-6(pg/ml)	**S**	**S**	**S**
IL-1β(pg/ml)	**S**	**S**	**NS**
IL-18(pg/ml)	**S**	**S**	**S**
IL-10(pg/ml)	**S**	**S**	**S**
IL-5 (pg/ml)	**S**	**NS**	**S** Lower

Significant value at (P<0.05),S: significant, NS: non-significant , S Lower: significant lower ,S-SLE: scabies-systemic lupus Erythematosus , S: scabies, C: control

Result in table (5) illustrate that the neutrophil and eosinophil have higher significant differences in scabies patients (42.9±6.20, 11.87± 3.0) as compare with control, while in scabies-SLE all leukocytes were lower significant difference as compare with control.

Table (5): Mean±SD for hematological parameters in all study groups

Parameters	Control n=20	Scabies n=22	Scabies-SLE n=12
Basophil %	0.5± 0.07	0.6±0.19	0.4±0.03
Neutrophil %	37.01±0.041	42.9± 6.20	35.3±0.02
Eosinophil %	4.989± 0.071	11.87± 3.0	3.243±0.02
Monocyte %	6.01± 0.196	6.1±34.1	5.04±0.154
Lymphocyte	33.021± 0.074	32.0±6.01	30.043±0.045

Table (6) shown that the SOD activity have higher significant differences in scabies patients (0.08±1.07), but lower significant differences in scabies-SLE (0.001±0.031) as compare with control. Level of MAD was higher significant in scabies-SLE (3.21±0.21) as compare with all others groups

Table (6): Mean±SD for oxidation parameters in all study groups

Oxidative stress parameters	Control n=20	Scabies n=22	Scabies-SLE n= 12
SOD Activity %	0.01±0.006	0.08±1.07	0.001±0.031
MAD(nmol/ml)	2.24±0.36	2.26±0.56	3.21±0.21

SOD: Superoxide dismutase, MDA: Malondialdehyde

Table (7) result illustrate that when compare between control and scabies groups the ratio of basophil, monocyte, lymphocyte and MAD were non-significant. But when compare between control and scabies-SLE all parametrs were lower significant except MAD. When compare between scabies and scabies-SLE all parameters were significant except SOD was lower significant.

Table(7):Significant and no significant value for hematological and biochemical parameters

Parameters	C vs. S	C vs. S-SLE	S vs. S-SLE
Basophil %	NS	S Lower	S
Neutrophil%	S	S Lower	S
Eosinophil %	S	S Lower	S
Monocyte %	NS	S Lower	S
Lymphocyte	NS	S Lower	S
SOD Activity	S	S Lower	S Lower
MAD	NS	S	S

Significant value at (P<0.05), S: scabies, S-SLE: scabies SLE

Discussion

Our study documented that the ratio incidence of scabies was high in female than male, also was high in children than adult and elderly, this result agree with other studies which found that Scabies, is more prevalent in children and young adults, and

more common in women than in men [11]. All patients were positive for IgG antibodies against *Sarcoptes scabiei* to insuring from the scabies infestation. Hs-CRP in scabies patients have significant differences at (p<0.05) as compare with control. The study showed that no significant differences in C3 and C4 values between scabies patients and controls. Most of the studies have indicated similar results [12]. Whereas in other study, C3 levels were elevated [13]. By the some studies there is suggestion that the scabies infections causing local deposition of C3 in the skin, so that induces a strong inflammatory response [14]. Perhaps the deposition of C3 in the skin, explains the decreasing in C3 level in scabies patients, presence of C3 has been documented in dermal blood vessels of scabies patients [15]. parasites which feeding Tissue and blood, face heavy threats by host innate immune responses, when Scabies mites feed on protein in epidermal and plasma, they will exposed to host defense mechanisms, internally and externally, recently, a family of multiple scabies mite homologues of the "group3 serine protease allergens", were described by molecular data [16]. The data identified 33 sequences, cluster into three classes, with all but one have mutations in the catalytic triad, eliminates the possibility of acting as proteases by any mechanism, 2 recombinant "scabies mite-inactivated protease paralogues (SMIPPs)" were demonstrated to inhibit the three pathways of the human complement [17]. The inhibitory action of both SMIPPs, occur by binding of three molecules involved in the three different mechanisms, that initiate complement pathway (properdin, C1q and mannose binding lectin), the 2 SMIPPs act as binding to the stalk domains of (C1q), then inhibiting C1r, C1s, which are associated to the same domain [18]. effects of these molecules in vivo are still unknown, the observed decreasing in the of levels of C3 and C4, in scabies patients, means the large inflammatory nature for this situation, and perhaps relate to higher levels of SMIPPs, which expressed by the millions of mites in the skin [19]. Scabies patients response to bites often by induce cell-mediated immune response, and humeral immune reactions, this study shown significant difference between IgG levels in scabies patients and control, this agree with Morsy *et al*.,(19) and disagree with other study by Burt *et al*.,2013 [20]. one animal study demonstrated that the antibody response in infested rabbits, was stronger than in immunized ones [21,22]. IgM levels were significantly higher in scabies patients than in controls, this agree with Yin *et al*.,2013[21], and disagree with Burt *et al*.,2013 [20]. The study observed a significant increase in IgA level in scabies patients as compared to the controls, this agree with Davidson *et al*.,2001[19] and disagree with Wahren *et al*.,2013[13]. The level of scabies specific IgA, which binding to a scabies mite recombinant protease, were significantly increased in scabies patient (WaltonS.F., unpublished data). The result of Immunohistochemistry documented that the Sarcoptes scabies proteases localizing in the gut of mite, which suggesting that they are involved in digestion of mite and skin burrowing, so it is possible, that the increased secretions of proteases into the skin by scabies mites, may induce the increasing levels of scabiei specific IgA [23]. There is higher significant in IgE levels in scabies patients as compare to control, this agree with Burt *et al*.,2013 [20]. IgE is consider the most important immunoglobulin in the host defense against scabies mites, and other parasites, staining of mite-infested skin

biopsies from scabies patients, has shown that IgG and IgE present in the gut of mite, also flooding the mite burrow [24] may be the changes in the levels of IgG, IgM, and in particularly IgE, refers to specific response to the parasite, or a nonspecific reaction to the dead parasite, or its debris and feces, or response to the secondary infection even [25]. some others suggested that the increasing levels of serum antibodies in scabies patients, may be associated with secondary infections, by other pathogens, Roberts *et al*., believed that the increased levels of total IgE and IgG, related to an inappropriate anti-inflammatory immune response by Th2 [26]. Kennedy documented the regulatory role, of IL-10 in inflammatory responses in patients with scabies [27]. Some researchers suggested that the IL-10, may be a natural regulator of mast cell activator, that reduces inflammation and irritability which related to allergic reactions, also they suggested that the IL-10 polymorphism, have relationship with increased level of IgE, and allergic reaction disease; so that IL-10 dis regulation may have effect on the type of allergic condition, patients with high level of IgE, may interfere with anti-inflammatory reaction of IL-10, then suffering from heavy allergic reaction [28]. All cytokines in present work (TNF-α, IFN-γ, IL-6, IL-1β, IL-18, IL-10 and IL-5) have higher significant differences in scabies patients as compare with control, Pro inflammatory cytokine appears to have effector role in the pathogenesis of scabies, some studies documented that IL-1β can production from the inflammation of skin, that caused by physical stimulation of the burrowing mites [29]. IFN-γ strong the inflammatory process, and not to improve the allergic immune response [30]. Bijjiga and Martino, suggested that minimizing the development of Th1-responses, is occur either by decreasing Th1- cytokines or encouraging Th2- cytokines [31]. The IL-10 is capable of inhibiting synthesis of the pro-inflammatory cytokines (IFN-γ and TNF-α), it have stimulatory role to certain T-cells and mast cells, also stimulates B-cell maturation and antibody production [31]. In this study IL-10 had higher significant differences in scabies patients, therefore immunoglobulin were higher in scabies than in control. IL-6 have both, proinflammatory and anti-inflammatory functions, IL-6 suggested plays proinflammatory roles in the scabies reaction, because it increase the vascular permeability, activate Th1CD4+cells to secrete IL-2, then promote their proliferation and differentiation, also IL-6 activate Th2CD4+ cells to produce IL-4, then drives antibody production, also the major cell infiltrate in the scabietic lesion is CD4+ cells, driven by IL-6 [32].Martino *et al*. suggested that the overproduction of immunoglobulin in some patients, might be by unbalanced of interleukin network and elevated IL-6 synthesis [33]. Gagari *et al*., sugessted that the IL-6 can induce through activation of mouse mast cells by stem cell factor, also the authors documented, that mast cells which produce IgE still a potential source of IL-6, also other cytokines which implicated in host defense, tissue maintenance, and other biological responses [34]. The increased level of IL-6 in this scabies patients like to be a responsible for increasing IgE production by the mast cells. The IL-6 role as an anti-inflammatory cytokine is mediated by its inhibitory effects on TNF-α [24]. the results of the current study suggested, that IL-6 acts as pro-inflammatory cytokine rather than a anti-inflammatory cytokine, due to not inhibition of TNF-α [28]. IL-5 is known to be associated with eosinophilic inflammation, so that it important in the terminal

differentiation of eosinophils, also important in survival, priming and activating of eosinophils [35,36]. Eosinophils percentage had higher significant differences in scabies patients as compare with control, the scabies patients in this study showed strong responses to the scabies antigens, so that most of scabies patients showed increased secretion of the Th2 IL-5, the results of this study show a significant increase in the number of neutrophils and eosinophil in scabies patients as compare with control, its likely the infection with this parasite causes stimulation for immune system of host, for both humeral and cellular. Some study documented that eosinophilia associated with scabies patients, this suggestion may be attributed to allergy disorder, which is one of symptoms of *S. scabiei* infection, or may be due to cellular response to the parasite infestation [37,38]. allergy causes increase in IgE antibody, then increase in the eosinophil because the receptor of IgE found on the surface of eosinophil and mast cell [39]. Prieto-Lastra, 2006; Onoja, 2013; Hiro, 2014 reported that the increasing eosinophil in patients with parasite, lead to produce some type of allergens, which may reach to a deeper layer of intestine mucosa, causing an increase in the number of eosinophils in scabies patients [38**].** Some others documented that Eosinophils, mast cells and basophils, are responsible for the initiation and regulation of Th2 responses, they can be reach faster to sites of infection and lymph nodes, where they produce IL-4 and IL-13 [40]. Section of Skin biopsy from scabies lesions, showed large numbers of infiltrating lymphocytes and eosinophils in the dermis, which enhanced production of IgE [41]. IL-5 is a key factor for promotes the maturation of eosinophils, Al-Dabbag (2006), documented that the early scabietic patients had higher eosinophils than the late ones [42]. This may be due to tolerance of the patients, or to the decrease in scabies severity [43]. Scabies patients have increased levels of SOD, this may refer to increase the free radical generation, so SOD increase to protect tissues from damage, this defense is highly effective, but it has limited capacity [44].The highest level of SOD indicate, that there is severe oxidative stress, this stress may have a role in the pathogenesis of scabies [43]. **While in Scabies-SLE patients,** Hs-CRP protein levels were significantly raised in scabies-SLE patients as compare with both control and scabies only, this result may refer to severe inflammation present in the scabies-SLE group, so the SLE is a different inflammatory process, that stimulate the acute phase protein response. patients with decreased cell-mediated immune responses have low serum complement, this may refers to presence of circulating antigen-antibody complexes in these patients, Antigen antibody complexes, have been shown to induce immunological hyporeactivity, through attachment to, and stimulation of, a subset of Fc-positive, concanavalin A-responsive T cells [45]. In scabies-SLE patients, IgG and IgA levels were higher significant than those in control, whereas the IgM levels were significant lower. a major feature of SLE is Hypergammaglobulinemia with elevations in serum IgM, IgG, and IgA levels [46]. SLE also consider a most common variable immunodeficiency [47]**.** some reports have documented there is an increase in serum IgM, during the early or active stages of the disease, [46]. patients with SLE for long duration, were found to have IgM deficiency, In these patients, the levels of serum IgA and IgG were increased, "a decrease in the level of IgM and an increase in

IgA may be reflective of immunologic alterations in SLE", Selective IgM deficiency, is consider a rare disorder associated with normal levels of immunoglobulins, but decrease in IgM levels [48]. All cytokines in this study have significant differences as compare with control and scabies patients except IL-5, IL-18 was significantly elevated in scabies-SLE patients as compare with both control, enhancement the expression of FAS ligand in NK cell and STL, induce by IL-18, causing FAS mediated apoptosis in epithelial cell and tissue damage, IL-18 in combination with other pro-inflamatory cytokines, must be an important cytokines, for initiation and progressing the catabolic response and fever in SLE [49]. T cells, neutrophils, and macrophages can be activated by Both IL-1 and TNF-α, then promote the expression of various inflammatory cytokines and mediators, some animal experiments suggested, that there is a significant positive correlation between the concentration of TNF-α which injected intravenously and the degree of kidney injury. TNF-α can induce chemotaxis and aggregation of leucocytes, the harmful effects of TNF-α on the kidney are similar to the effects of endotoxin [50]. In the scabies, scabies-SLE and scabies-psoriasis we showed that the serum level of TNF-α increased significantly, in our opinion, scabies can induce other disease, perhaps by mediated the immune and inflammatory responses, which induced by a variety of *S. scabiei* antigens or by development secondary infections of skin, so that scabies leads to serious pruritus. The mites under the cuticle can produce soluble antigens; like feces, saliva, dead and disintegrated mites or other secretions, dead and disintegrated mites, have greater pathogenic effects in inducing inflammatory responses by the human body, than live mites, through subcutaneous intercellular fluid, antigens can spread to the dermis, and stimulate immune responses [52]. Some others suggested that the extracts of dead or live mites, can influence the number of inflammatory cells in local tissues, and blood during immune responses of the host, soluble antigens some of which can migrate, and localize in the glomerulus via the circulation, then form situ antigens, which form immune complexes by interacting with specific antibodies, and accumulate in the glomerulus to induce kidney lesions [53]. We supposed that the pathogenesis of SLE induced by scabies, including the binding of S. scabiei specific IgG to the Fc binding protein in the host cell, through its Fc and then deposition of IgG complex in the blood vessel and tissues, this complex can activate the complement, inflammatory cells and induce the release of a variety cytokines to cause tissue damage. "Neutropenia in patients with SLE can result from immune mechanisms, bone marrow dysfunction, or hypersplenism" [54]. Lymphocytopenia, has been observed in patients SLE, particularly during active disease [55]. This is strongly associated with complement fixing, and presumably cytotoxic antilymphocyte antibodies [56]. The number of basophils may also be decreased in SLE, during active disease [57]. MAD was higher significant in scabies-SLE patients as compare with control and scabies only, suggest an increased lipid peroxidation, and active role of lipid peroxidation in the pathogenesis, and progression of SLE. "Increased lipid peroxidation has previously been detected in SLE, but the significance of lipid peroxidation in the initiation and development of SLE remains largely unexplored", Human cells have both enzymatic and non-enzymatic antioxidant defense systems, SOD, a major

enzyme and consider the first line of defense against oxygen-derived free radicals, any changes in this normal balance of oxidant, likes elevated of ROS production and decreased antioxidant levels, causing oxidative stress [58,59]. SOD levels were significantly lower in the scabies-SLE patients as compare with control, this may refer to the heavy inflammatory response in these patients.

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