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Seasonal distribution and correlation between IL-10 and IL-13 gene polymorphism and their expression in scabies-infected patients

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Abstract

Scabies is a significant concern in global health. It is more prevalent in individuals who have poor hygiene and live in crowded conditions, hence, it is seasonal distribution and immunological response in Erbil population is the aim of the present study. In the Erbil Dermatology Education Centre in Erbil, Iraq, 154 patients were recruited for the research between April 2022 and March 2023. If a patient has a suspicious skin lesion and itching for a minimum of one week, scabies may be considered. Blood samples were collected from each participant in the study to evaluate serum levels of IL-10 and IL-13, then the DNA was isolated to study the gene polymorphism for the mentioned cytokines. Results showed that female 60.3% were more infected than male 39.6%. The median age of participants was (10 - >51) years, among infested, adolescents aged 10-20 years displayed the highest rate (31.8%). The carriers of GA genotype of IL-10 were protective against the infection, OR:0.61. while the TT carriers of IL-13 were susceptible to scabies infection with OR:2.14. IL-10 GA genotype was more prevalent in male patients OR:2.14 whereas the AA genotype was most protective in females OR:0.32. the IL-13 CT genotype was protective for males with OR:0.52. Both of IL-10 and IL-13 serum levels were increased significantly with infection and highest levels were found in wild homozygous genotypes (GG and CC) and lowest ratio was found in mutant homozygous genotypes of IL-10 and IL-13 respectively. Point mutation in IL-10 GA was protective and wild TT genotype of IL-13 was susceptible to the scabies infection. Double mutation in IL-10 AA was protective to females and single mutation of IL-13 CT was protective to males.

Keywords: Scabies, Seasonal distribution, IL-10 GA, IL-13 CT, Cytokine gene polymorphism

1. Introduction

Scabies is a significant concern in global health, characterized by the presence of Sarcoptis scabiei var. hominis, an oval-shaped, ventrally compressed mite adorned with dorsal spines. Following fertilization, the female mite penetrates the stratum corneum to deposit her eggs. Burrows, skin abrasions, and pruritic raised skin lesions are notable manifestations of scabies. Areas such as the lower abdomen, genitalia, buttocks, axillae, finger webs, wrists, and areolae are commonly affected [1]. It is more prevalent in individuals who have poor hygiene and live in crowded conditions. It also affects persons of all ages and both sexes, regardless of their financial status and degree of hygiene [2].

Due to the extremely itchy lesions created by the infestation, there may be secondary infections and significant pain. It spreads in homes and other places where people have close personal touch [3]. Due to its prevalence in a variety of domestic and wild animals, including dogs, pigs, cattle, small ruminants, camelids, and rabbits, S. scabiei is also extremely important for veterinarians [4].

In addition to inanimate items (clothes and furniture), direct skin contact between members of the same household can also spread scabies. Sexual contact is another crucial way for adults to get the disease [5]. Moreover, scabies has been the subject of increased public attention in recent years, and the World Health Organization (WHO) designated scabies as a Neglected Tropical Disease (NTD) in 2017 [6].

Numerous epidemiological characteristics, such as age, sex, ethnicity, overcrowding, cleanliness, and season, can affect the spread of scabies infestation in communities. It was formerly believed that the prevalence of scabies was cyclical; however, research on long-term incidence indicates that epidemics and other apparent oscillations are multifactorial, linked to social and environmental factors like wartime, overcrowding, and changes in climate [7].

Scabies is often transmitted as a result of both natural and man-made critical incidents, such as war, floods, earthquakes, and other similar occurrences. The prevalence of scabies can vary depending on the specific location, ranging from 0.4% to 50%. Certain population-based studies have determined that a minimum of 3.3% of the population in Basrah, located in the southern region of Iraq, is

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at risk. In Tikrit, which is situated in the central region, the percentage is 1.2%, while in Samara, located in the center, it is 1.9%. In Kirkuk, situated in the northern region, it is 2.7%. The province of Babylon has a scabies frequency of 14.32% [8]. Furthermore, data from Dohuk in northern Iraq has revealed an infection rate of 5.5% for scabies [9].

There is a dearth of studies on immunological alterations that take place in the human systemic immune response, despite the availability of data on human immunity against scabies. According to a previously conducted study, the most prevalent cells near the lesion site are inflammatory cells (lymphocytes, macrophages, and eosinophils) [10]. To get rid of the mites, eggs, and detritus, the skin's cell-mediated immune response and the bloodstream antibody response work in tandem. While there is ample evidence of a T-cell-mediated immune response to scabies, there is little information available on the humoral immune response [11].

The immune system's Th1/Th2 balance is distorted by scabies mite invasion [12]. Because scabies secretes cytokines, T-lymphocytes (T-cells) specifically CD4+ T-helper (Th) and CD8+ T-cytotoxic (Tc) play a significant role in the immune response. T-helper cells produce IL-13, IL-5, and IL-4, which stimulate the creation of antibodies to combat external parasites and mediate humoral immunity [13].

The IL-10 gene maps to the junction of 1q31–q32 [14] and this gene is highly polymorphic with a number of single nucleotide polymorphisms in the promoter region, in addition there is 3 polymorphic susceptible sites found in IL-10 promoter region including -1082(G/A), -592(C/A) and -819(C/T) [15].

Additionally, mast cells, basophils, eosinophils, and T-cell subsets generate the immunoregulatory protein IL-13. Given that its levels and genetic polymorphism variations have been linked to higher blood IgE levels in atopic and asthmatic patients of various ethnic origins, it is thought to be a significant mediator in allergic illness [16].

Taking into account genetic variants found in cytokine-encoding genes, IL10 -1082 G>A single nucleotide polymorphisms (SNPs) were linked to scabies [17]. Single-nucleotide polymorphisms (SNPs) in IL-4 and IL-13 have been found in allergy sufferers from many different nations. While negative consequences have been observed, asthma patients have exhibited gene-gene interactions among these genes. The aim is to examine the interplay between these genes as well as the SNPs within them in relation to atopic dermatitis [18]. There is another SNP for the IL13 gene, rs1295685, which is strongly linked to rs20541. The haplotypes of this SNP are linked to AD and total blood IgE levels [19]. This study aimed to ascertain the seasonal pattern of scabies cases, along with the occurrence of scabies within the populace of Erbil. Furthermore, the inquiry employed ARMS-PCR methodology to probe the correlation between the interleukin-10 (1082 G/A) and interleukin-13 (1046F C/T) promoter polymorphisms in a particular subgroup of scabies-afflicted individuals in Erbil.

2. Materials and Methods

2.1. Sampling

In the Erbil Dermatology Education Centre in Erbil, Iraq, epidemiological notification for the patients visited between April 2022 and March 2023, a total of 305 infestations were detected, from them 154 patients were recruited for the immunological research (After excluding young and very old ages as well as co-infections). If a patient has a suspicious skin lesion and itching for a minimum of one week, scabies may be considered. Dermatologists verified that the samples were contaminated. Consent was obtained from each patient and a questionnaire form was created with their personal information (age, residence, socioeconomic situation, etc.). Fifty-one healthy individuals in the same age range as the patients were chosen as controls.

2.2. Blood samples

Venous blood samples of 7 ml were collected from each participant in the study. The blood was then divided into two equal portions, with the first portion (5 ml) being dispensed into a plain tube. Subsequently, it was subjected to centrifugation at a speed of 3000 revolutions per minute for 15 min, using a temperature-controlled centrifuge set at 4°C. After centrifugation, the resulting serum was divided into three smaller portions and transferred to Eppendorf tubes. These aliquots were then frozen at a temperature of -20℃, and preserved until the time of analysis for hormone and cytokine serum levels. In parallel, the second portion of the blood sample (2 ml) was transferred to an EDTA tube and also frozen at -20℃, to facilitate the subsequent extraction of DNA for genotyping of IL-10 and IL-13 gene polymorphisms.

2.3. Laboratory investigations

2.3.1. A.Immunological assays

The ELISA was used to determine the levels of IL-10 and IL13 in accordance with the manual technique of kits supplied by Bioassay Technology Laboratory UK.

2.3.2. B. DNA extraction and genotyping

Following the manufacturer's instructions, the genomic DNA was separated and extracted from the venous blood of the investigated samples (PureLinkTMGenomic DNA Mini Kit).

To determine the IL-10 genotype at (-1082 G/A) (rs1800896), experiments were performed in a reaction volume of 20 ZL. 40 ng of genomic DNA, 1.5 mM dNTPs, 25 mM $MgCl_2$, 1 µL of 10 pmol primers, and 0.4 units of Taq polymerase (Fermentas, Maryland, USA) in 1X Reaction Buffer made up the reaction mixture. Table 1 lists the primers that were used to amplify the various polymorphisms. The polymerase chain reaction (PCR) was carried out in a thermal cycler (PX2) under the following cycling conditions: initial denaturation at 95 °C for 3 min, followed by 35 cycles at 95°C for 45 sec, 58°C for 40 sec, 72 °C for 1 min, and a final extension at 72 °C for 7 min. The amplicon that was produced was 254 bp in size. The amplified products were then subjected to analysis on a 2% agarose gel.

Genotyping of IL-13-1112 C>T: The allele-specific PCR technique (ARMS-PCR) was used to identify the IL-13 gene polymorphism -1112C>T (rs1800925). Table 2 provides a summary of the primer set used to amplify different kinds of polymorphisms. The reaction mixture comprised 5 µl of each primer and 12 µl Dream Taq DNA Master Mix (2X, Fermentas, K1081, USA) in a final volume of 25 µl. The amplification process was carried out using a thermal cycler, with two minutes at 94°C, fifteen cycles of

Table 1. Primers of IL-10(-1082 G/A).

IL-10(1082 G/A)	Sequences	Product size
anti-sense primer	5'-CAG TGC CAA CTG AGA ATT TGG-3'	
Sense primer G	5'-CTA CTA AGG CTT CTT TGG GAG-3' 258	258 bp
Sense primer A	5'-ACT ACT AAG GCT TCT TTG GGA A-3'	

Table 2. Primers of IL-13(1046F).

IL-13 -1046F	Sequences	Product size
anti-sense primer	5′GGAGATGGGGTCTCACTATG3	
Sense primer C	5′TTCTGGAGGACTTCTAGGAAAAC3′	400 bp
Sense primer T	5′TTCTGGAGGACTTCTAGGAAAAT3′	

30 s at 94°C, sixty seconds at 63°C, sixty seconds at 72°C, twenty cycles of 30 s at 94 °C, sixty seconds at 60 °C, and sixty seconds at 72°C, and lastly, five minutes at 72°C. 400 bp is where the band appears in the PCR products, which were separated on a 2% agarose gel.

2.4. Statistical analysis

The statistical software SPSS 26.0 (SPSS Inc., Chicago, IL, USA) was used for all analyses. Mean ± SD was used to express normally distributed variables. P<0.05 was designated as the level of statistical significance. The presentation of descriptive data was given as mean ± standard deviation (SD). Utilizing 2x2 contingency tables, z statistics, and a ($\chi 2$)-test of independence, genotype, and allele frequencies were compared between the groups. The level of statistical significance was set at P<0.05.

2.5. Epidemiological criteria

The epidemiological criteria of the present study were according to [20].

3. Results

A total of 305 infestations were recorded among people living in Erbil Province, with overall of infestation prevalence 1.12% (Table 3), its environs and villages that visited Erbil Dermatology Education Centre participated in the study (Among the patients a total of 154 were investigated for immunologic study). In the province of Erbil as shown in Table (3) illustrates the distribution of study participants by season, which indicates a higher number of patients in the summer and spring than in the winter and fall.

The present study results showed that female 60.3% were more infected than male 39.6%. The median age of participants was (10 - >51) years, among infested, adolescents aged 10-20 years displayed the highest rate (31.8%),. Most patients were free workers (68.8%) was appeared in Table (4).

In this study more than half of the patients were live in rural (61%) and most of them were poor. More than half of the patients were married (61.6%). The most common symptom of the disease was itching (100%), especially at night.

Regarding the IL-10-1082G/A genotypes, the high producer GG carriers were not significantly increased in patients with OR: 1.59 (C.I%: 0.37-9.54). While the GA intermediate producer was found to decrease none signi-

Table 3. The significant differences in the seasonal distribution of scabies infestation rates (calculated p = 16.226 and tabulated p = <.001).

Months	Season	All Patients	Scabies cases	Prevalence (%)
December		1776	19	1.06
January	Winter	2032	10	0.49
February		1528	8	0.52
		5336	37	**0.69**
March		3128	48	1.53
April	Spring	2840	35	1.23
May		2936	24	0.81
		8904	107	**1.19**
June		2488	43	1.72
July	Summer	2760	35	1.26
August		2808	36	1.28
		8056	114	**1.41**
September		2248	35	1.55
October	Autumn	1688	7	0.41
November		808	5	0.61
		4744	47	**0.99**
Overall		**27040**	**305**	**1.12**

Table 4. Socioeconomic characteristics of the study sample.

Variables	Categories	Patient (n=154)	Control (n=51)
Sex	Male	61(39.6%)	22(43.1%)
	Female	93(60.3%)	29(56.8%)
Age	10 - 20	49(31.8%)	14(27.4%)
	21 -30	24(15.5%)	11(21.5%)
	31 - 40	26(16.8%)	10(19.6%)
	41 - 50	15(9.7%)	6(11.7%)
	>51	40(25.9%)	10(19.6%)
Occupation	Employee	29(18.8%)	34(66.6%)
	Free worker	81(52%)	6(11.7%)
	Student	44(28.5)	10(19.6%)
Adders	Rural	94(61.0%)	
	Urban	60(38.9%)	51(100%)
Marital tatus	Single	59(38.3%)	6(11.7%)
	Married	95(61.6%)	44(86.2%)
Symptoms	Rash	64(41.5%)	
	Crusted	59(38.3%)	
	Itch	154(100%)	
	Redness	114(74.0%)	

Table 5. IL10 and IL13 SNP genotypes and allele frequencies with dominant impact in the patients and control.

Genotypes and Allele frequency	Patients N=94 (%)	Control N=48 (%)	OR	95% C.I	P value
IL-10					
GG	63(67%)	29(60%)	1.33	0.60 to 2.90	0.275
GA	22 (23.4%)	16 (33.3%)	0.61	0.27 to 1.43	0.144
AA	9(9.6%)	3(6.3%)	1.59	0.37 to 9.54	0.327
G	40 (21.3%)	22 (22.9%)	0.91	0.49 to 1.73	0.431
A	148 (78.7%)	74 (77.1%)	1.1	0.58 to 2.06	0.431
IL-13					
CC	54 (57.5%)	27 (56.25%)	1.05	0.49 to 2.24	0.516
CT	32 (34%)	19 (39.6%)	0.79	0.36 to 1.73	0.319
TT	8 (8.5%)	2 (4.2%)	2.14	0.40 to 21.40	0.28
C	140 (74.5%)	73 (76%)	0.92	0.49 to 1.68	0.446
T	48 (25.5%)	23 (24%)	1.09	0.59 to 2.03	0.446

ficantly in patients, the OR: 0.61 (C.I%: 0.27-1.43). The presence of AA low producer was increased none significantly in patients than controls with OR: 1.33 (C.I%:0.6-2.9). The point mutation heterozygous G to A in one allele in IL-10-1082 SNP was considered remarkably a protective factor with the infection of scabies. Moreover, the wild and mutant homozygous carriers were at risk of the infection as appeared in Table 5.

Moreover, about the IL-13 C/T genotypes, the higher producer CC almost has the same presence about 57% in the patients and controls, OR: 1.05 (C.I%: 0.49-2.24). The CT producers were found less in patients with OR: 0.79 (C.I%: 0.36-1.73). The TT low producers were more than double folded increased in patients than controls, OR: 2.14 (C.I%: 0.4-21.4). The presence of T in both alleles is remarkably a risk factor for scabies infection. was appeared in Table 5.

When comparing the genotype differences between male and female patients appeared in Table (6), the results showed following records. The GG genotype was decreased in male patients OR: 0.32 (C.I%: 0.03-1.84) and this genotype was considered as a risk factor for females and protective factor for males. While GA genotype carriers were increased more than 2-fold in male patients with OR: 2.14 (C.I%: 0.73-6.44) and it is a risk factor for males to have the scabies infection. In male patients, the AA genotype of IL-10-1082G/A was lower (OR: 0.8; C.I%: 0.31-2.08). The G allele carriers are protective for males and risk for females, whereas the A allele carriers were contrary to the G allele.

Another studied SNP was IL-13C/T gene polymorphism between male and female of the selected patients was appeared in Table (6) The CC genotype was increased in male patients with OR: 1.67 (C.I%: 0.67-4.19). The CT intermediate producers were decreased in male patients and it is found to be a protective factor against this type of infection with OR: 0.52 (C.I%: 0.19-1.37). The low producers TT genotype was also increased with no remarkable interest in male patients, OR: 1.26 (C.I%: 0.22-7.24).

Table 7 results showed that there were substantial ($P<0.05$) variations in the levels of IL-10 between the patient groups and the control group. Specifically, the levels of IL-10 in the infected patients' groups reached 55.6±6.4 pg/ml, while the control group's levels were 37.4±7.9 pg/ml. There were notable differences ($P<0.05$) in the mean blood IL13 levels between the scabies-infested patient's 110.23±16.8 pg/ml and the control patient's 71.26±14.32 pg/ml.

Table (8) displays the correlation between the IL-10 genotype (1082 G/A) and the IL-10 levels within both the patient and control groups. The results indicated that individuals with the G allele (G/A heterozygotes or G/G homozygotes) exhibited significantly elevated serum levels of IL-10. Specifically, the GG genotype manifested IL-10 levels of 61.54±9.43 and 38.84±6.78 pg/ml in the patient and control groups, respectively, whereas the GA genotype displayed levels of 54.89±8.78 and 36.81±8.46 pg/ml, respectively. Conversely, patients possessing the A allele (AA homozygote mutant type) displayed diminished blood levels of IL-10; in the case of the AA genotype, these levels were 50.34±10.24 and 36.53±9.56 pg/ml in the patient and control groups, respectively.

Additionally, Table 8 shows the relationship between the IL-13 C/T genotype and the amount of IL-13 in the patient and control groups. According to the results, patients who carry the C allele (C/T heterozygotes or C/C homozygotes) have statistically higher serum levels of IL-13. For example, the CC genotype showed IL-13 levels in the patient and control groups of 135.54±21.1 and 78.23±12.34 pg/ml, respectively, while the CT genotype showed 105.62±16.65 and 70.12±14.65 pg/ml, respectively. Conversely, patients with the T allele (TT homozygote mutant type) had lower blood levels of IL-13; for the TT genotype, the levels in the patient and control groups were 89.63±20.2 and 65.45±16.21 pg/ml, respectively.

4. Discussion

In third-world nations, scabies is regarded as one of the most common skin illnesses. About 300 million people worldwide are afflicted with scabies annually, and an estimated 130 million people are affected at any one period of time. The majority of these occurrences occur in developing nations among impoverished individuals who reside in congested, rural, and tropically climate-characterized places [21]. According to this study, 10.2% of the province of Erbil had scabies. Research on the prevalence of scabies in Kurdistan is scarce. Barwari [22] found that the prevalence of scabies among residents of 35 camps was 4.5%. In contrast, Hassan and Mero [23] found that the rate of scabies among internally displaced persons residing in five camps near Duhok, Kurdistan, Iraq, was 10% (395/3,925). Of the 154 patients with scabies, 61 patients (39.6%) were men and 93 patients (60.3%) were women.

In terms of seasonal changes in infestation, it is evident that there is a considerable rise in patients during the summer and spring as opposed to the winter and fall. This finding is consistent with research conducted in the Iraqi province of Thi-Qar by Mousa and Hassan [17]. Prior research has demonstrated that the primary climatic element influencing the risk of scabies infection is temperature [22]. Many poor nations are home to the endemic

Table 6. The genotypes and allele frequency of the IL-10AG and IL-13CT in male and female patients.

Genotypes and Allele frequency	Male Patients N=42 (%)	Female Patients N=52 (%)	OR	95% C.I	P value
IL-10					
GG	27(64.3%)	36(69.2%)	0.8	0.31 to 2.08	0.386
GA	13 (31%)	9 (17.3%)	2.14	0.73 to 6.44	0.096
AA	2(4.7%)	7(13.5%)	0.32	0.03 to 1.84	0.141
G	67 (79.8%)	81 (77.9%)	1.12	0.52 to 2.43	0.448
A	17 (20.2%)	23 (22.1%)	0.89	0.41 to 1.91	0.448
IL-13					
CC	27 (64.3%)	27 (52%)	1.67	0.67 to 4.19	0.160
CT	11 (26.2%)	21 (40.4%)	0.52	0.19 to 1.37	0.110
TT	4 (9.5%)	4 (7.6%)	1.26	0.22 to 7.24	0.517
C	65 (77.4%)	75 (72.1%)	1.32	0.65 to 2.74	0.257
T	19 (22.6%)	29 (27.9%)	0.76	0.36 to 1.55	0.257

Table 7. The levels of IL10 and IL13 pg/ml in patients and control groups.

Parameters	Patients	Control	P value
IL-10	55.6±6.4	37.4±7.9	0.033
IL-13	110.23±16.8	71.26±14.32	0.039

Table 8. The relationship between the patients' and controls' levels of IL-10 and IL13 (pg/ml) and their genotypes of IL-13 C/T and IL-10 (1082 G/A).

Serum level/ Genotype	Patients	Control	P value
IL-10			
GG	61.54±9.43	38.84±6.78	0.023
GA	54.89±8.78	36.81±8.46	0.039
AA	50.34±10.24	36.53±9.56	0.06
IL-13			
CC	135.54±21.1	78.23±12.34	0.03
CT	105.62±16.65	70.12±14.65	0.047
TT	89.63±20.2	65.45±16.21	0.70

Sarcoptes scabiei mite, which is most prevalent in hot, humid climates. High temperatures have a significant impact on the mites' accelerated demise and droughts [24]. In contrast, mites have a higher chance of surviving in colder climates and have higher fertility rates. However, the current study's prevalence results were higher in warm seasons because host-detached parasites have a higher chance of surviving, which means that new infestations will occur more frequently. The majority of severe cases were observed in the winter and late autumn [17].

Research indicates that scabies mites may survive up to 19 days in a chilly, humid environment, whereas they can only survive 1.5 days on the host body in typical indoor settings. However, when the mites migrate from one location to another, higher temperatures ensure the occurrence of new infestations [24]. The majority of the cases in this study were in the summer and spring, and although research on scabies in developed nations describes the disease's outbreak during cold weather in the winter, these seasons also represent the best times for travel and recreation in Iraq, so public settlements such as hotels and other establishments may be the source of the outbreak. Additionally, religious visits during these seasons may have contributed to the outbreak.

According to Table 1 of this study, there was a higher incidence of scabies among females. This is likely because females tend to have closer physical contact with their family members, especially in large family units, which facilitates transmission and indirectly explains why different rates of scabies spread according to age and sex. Infested individuals can indirectly spread scabies via sharing mite-contaminated clothing, bedding, bed linens, furniture, shared hats, and head coverings, in addition to direct skin-to-skin contact [25, 26]. However, in additional research, it was discovered that men and women were equally impacted [27].

There is a complicated link between socioeconomic status and scabies infestation. According to this study, there was a higher incidence rate of scabies (52.5%) in correlation with an increase in the unemployment rate (free workers). Additionally, prior research has demonstrated a correlation between family income and the disease's frequency [28, 29].

According to the present study findings, the percentage of scabies infections in rural and urban regions was 61% and 38.9%, respectively. These findings are consistent with [30], which establishes that, of the 2104 schoolchildren who contracted scabies, 862 (41%) resided in urban areas and 1242 (59%) in rural regions in Kafr El-Sheikh, Egypt. Lately [31].

In Iran, the rural communes showed a greater incidence [32]. The worse economic, hygienic, and sanitary conditions of the rural populace might be the cause of this phenomenon. It could also be brought on by less health education and more restricted access to medical treatment [33].

The levels of IL-10 in the two study groups varied significantly from one another. According to Abd el-aal *et al.* [34], there was a notable difference in IL-10 levels between the patient and healthy groups, with the latter group having levels as high as 269±112 pg/ml. Additionally, IL-10 and other anti-inflammatory Th2 cytokines may be protective against severe manifestations of human scabies.

The results of this study suggest that IL-10 functions as a natural regulator of mast cell activators, lowering inflammation and irritation associated with allergic responses. According to Arlian *et al.* [35], scabies mites secrete IL-10 and TGF-β, which encourage the development of regulatory T cells and prevent an inflammatory or immunological response to the parasite, perhaps postponing the host's initial immune response.

When comparing the mean serum IL-13 levels of scabies-infested patients to controls, a significant difference ($P \leq 0.05$) was noted; these results were consistent with those reported by Mohammad *et al.* [36]. Pro-inflammatory Th2 cytokines, such as IL-13, enhance the generation of antibodies to combat extracellular parasites, hence mediating humoral immunity [29].

The concept seems to be increasingly supported by the inflammatory reaction that underlies atopic dermatitis, where IL-13 is locally overexpressed and significantly affects skin biology through changes to the skin microbiome, the recruitment of inflammatory cells, and the breakdown of the epidermal barrier [37].

The current study found that while genotypes GG and AA of the IL-10 (1082 G/A) polymorphism were not significantly higher, genotype GA was lower in Scabies patients than in the controls. This suggests that the IL-10 (−1082 G/A) polymorphisms are associated with a higher risk of Scabies and may act as a protective factor for IL-10 [38].

The polymorphism of IL-10 (1082 G/A) and IL-13 (1046F) in scabietic patients has been the subject of relatively few investigations; as a result, the data from the current study was compared to individuals with psoriasis and atopic dermatitis as dermatologic illnesses.

According to Reich *et al.* [39], it has been observed that the IL-10 genotype of the Macedonian population, specifically (−1082 GA), makes them more prone to developing atopic dermatitis. Conversely, the IL-10 genotype (−1082

AA) has a protective effect against this condition. It is believed that the IL-10-1082 G allele is associated with an increase in IL-10 production from peripheral mononuclear cells.

Polymorphisms in the IL-10 gene coding genes are likely a contributing factor to psoriasis susceptibility, according to other research conducted on the English population [40]. However, Kingo et al. showed that the Estonian population's IL-10 haplotype influences the degree and course of psoriasis [41].

The minor TT genotype in the current investigation about the IL-13 C/T genotypes was shown to be substantially associated with an elevated risk of scabies; this finding was consistent with that reported by Miyake *et al.* [42].

Atopic dermatitis (AD) has been linked to SNPs in the IL-13 gene through several association studies [43]. These investigations have revealed that the filaggrin mutation, both by itself and in conjunction with specific IL-10 or IL-13 polymorphisms, increased the incidence of AD in the Polish population. Research suggests a relationship between the prevalence of AD in the Danish population and a polymorphism variation of the IL-13 gene [44]. Numerous studies have demonstrated the function of proinflammatory cytokines, such as interleukin IL-10 and IL-13, in the immune response against scabies [10].

The present study discovered that certain gene variations in cytokine genes IL10 and IL13 may serve as genetic markers for susceptibility and/or severity of Scabies among our cases. The study's findings revealed significantly higher levels of IL-10 serum among carriers of the G allele (G/A heterozygotes or G/G homozygotes vs. A/A homozygotes) in the -1082 G/A IL-10 polymorphism in scabietic patients compared to control groups. Lesiak *et al.* [45] conducted a study on IL-10 serum levels and IL-10 (1082 G/A) polymorphism in AD patients and proposed the involvement of the G allele in IL-10 synthesis in patients with moderate to severe AD. Nonetheless, IL-10, being an immunosuppressive cytokine, hinders the activity of Th1 and Th2 cell types in human subjects.

Also, Napolitano *et al.* [46] demonstrated that mucosal IL-10 mRNA was greater in carriers of the IL-10 -1082G gene than in carriers of the IL-10 -1082A variant. The results of this study demonstrate that IL-10 is both immunosuppressive in groups infected with a virus for the first time and protective in groups infected with a virus again. Furthermore, individuals with GG and GA genotypes with high IL-10 production are those whose transcription factors have a strong association with the mRNA of the G allele and a weak association with the mRNA of the A allele.

According to the current study's findings, scabietic patients with the C/T IL-13 polymorphism had significantly higher blood levels of IL-13 than control groups if they were carriers of the C allele (C/T heterozygotes or C/C homozygotes vs. T/T homozygotes). As far as is currently understood, AD is partly thought to be a Th2-derived illness, and IL-13 plays a significant role in the development of allergic inflammation. A high level of these cytokines in the blood is seen in some cohorts of AD patients, which is likely influenced by genetic background [43]. IL-13 may have a significant role in the pathophysiology of AD, according to recent research. It plays a major role in triggering type-2 T-helper inflammation and is overexpressed in AD patients' lesional skin[47].

Conflict of Interests

There are no conflicts between the author and any stage of the essay production.

Consent for publications

The author reviewed and gave her approval for the final manuscript.

Ethics approval and consent to participate

Ethical Approval was taken in Salahaddin University councel for research.

Informed Consent

Consent was taken for each patient.

Availability of data and material

All data will be available upon reasonable request.

Authors' contributions

This study is a part of PhD thesis, Eman Farhad Bilal did the research study with the supervisors collaboration.

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References

1. Lugović-Mihić L, Delaš Aždajić M, Kurečić Filipović S, Bukvić I, Prkačin I, Štimac Grbić D, et al (2020) An increasing scabies incidence in Croatia: A call for coordinated action among dermatologists, physicians and epidemiologists. Zdr Varst 59 (4): 264–272. doi: 10.2478/sjph-2020-0033.
2. For the Western Pacific WHORO (2020) Programme Managers Meeting to Accelerate Control and Elimination of Neglected Tropical Diseases in the Western Pacific Region, Virtual meeting, 1-4 September 2020 : meeting report. 35 p.
3. Burns DA (2010) Diseases Caused by Arthropods and Other Noxious Animals. Rook's Textb Dermatology Eighth Ed 2 1757–1817. doi: 10.1002/9781444317633.ch38.
4. Guillot J, Losson B, Delsart M, Briand A, Fang F, Rossi L (2023) Sarcoptic Mange in Wild and Domestic Animals. In: Scabies. Springer. pp 313–343.
5. Sarker SC, Nath SK, Al Miraj AK, Chowdhury MAH, Firoz AMA (2022) Prevalence and Life Cycle in Patients with Scabies Infection-A Study in Kumudini Women's Medical College Hospital, Tangail, Bangladesh. Glob Acad J Med Sci 4 (5): 224–229. doi: 10.36348/gajms.2022.v04i05.004.
6. Aždajić MD, Bešlić I, Gašić A, Ferara N, Pedić L, Lugović-Mihić L (2022) Increased Scabies Incidence at the Beginning of the 21st Century: What Do Reports from Europe and the World Show? 12 (10): 1598. doi: 10.3390/life12101598.
7. Gupta DK, Singh RP, Singh AK, Agarwal AK, Kumar A, Gava U (2021) Study of prevalence and determinants associated with scabies in rural area of Bareilly. Indian J Community Heal 33 (1): 169–174. doi: 10.47203/IJCH.2020.v33i01.023.
8. Al-Jassani MJ, Al-Lamy NA, Kadhim AJ, Hammood GA (2023) Incidence of Human Scabies in Babylon Province, Iraq. Int J Pharm Qual Assur 14 (1): 87–90. doi: 10.25258/ijpqa.14.1.15.
9. Mero W, Hassan H (2014) Incidence of Human Scabies in Duhok Province, Kurdistan Region/ Iraq. Sci J Univ Zakho 2 (2): 285–292. doi: 10.25271/2014.2.2.203.
10. Bhat SA, Mounsey KE, Liu X, Walton SF (2017) Host immune responses to the itch mite, Sarcoptes scabiei, in humans. Parasit Vectors 10 (1): 385. doi: 10.1186/s13071-017-2320-4.

11. Arlian LG, Fall N, Morgan MS (2007) In vivo evidence that Sarcoptes scabiei (acari: Sarcoptidae) is the source of molecules that modulate splenic gene expression. J Med Entomol 44 (6): 1054–1063. doi: 10.1603/0022-2585(2007)44[1054:IVETSS]2.0.CO;2.
12. Lalli PN, Morgan MS, Arlian LG (2004) Skewed TH1/TH2 immune response to Sarcoptes scabiei. J Parasitol 90 (4): 711–714. doi: 10.1645/GE-214R.
13. Walton SF, Pizzutto S, Slender A, Viberg L, Holt D, Hales BJ, et al (2010) Increased allergic immune response to Sarcoptes scabiei antigens in crusted versus ordinary scabies. Clin Vaccine Immunol 17 (9): 1428–1438. doi: 10.1128/CVI.00195-10.
14. Liu Q, Yang J, He H, Yu Y, Lyu J (2018) Associations between interleukin-10 polymorphisms and susceptibility to rheumatoid arthritis: a meta-analysis and meta-regression. Clin Rheumatol 37 (12): 3229–3237. doi: 10.1007/s10067-018-4329-2.
15. Smith AJP, Humphries SE (2009) Cytokine and cytokine receptor gene polymorphisms and their functionality. Cytokine Growth Factor Rev 20 (1): 43–59. doi: 10.1016/j.cytogfr.2008.11.006.
16. Liu X, Walton SF, Murray HC, King M, Kelly A, Holt DC, Currie BJ, Mccarthy JS, Mounsey KE (2014) Crusted scabies is associated with increased IL-17 secretion by skin T cells. Parasite immunology, 36, 594-604.
17. Mousa HM, Hassan AG (2020) Scabies infection in thi-qar province. Syst Rev Pharm 11 (5): 106–109. doi: 10.31838/srp.2020.5.17.
18. Namkung JH, Lee JE, Kim E, Kim HJ, Seo EY, Jang HY, et al (2011) Association of polymorphisms in genes encoding IL-4, IL-13 and their receptors with atopic dermatitis in a Korean population. Exp Dermatol 20 (11): 915–919. doi: 10.1111/j.1600-0625.2011.01357.x.
19. Lee E, Kim JH, Lee SY, Kang MJ, Park YM, Park MJ, et al (2020) Association of IL13 genetic polymorphisms with atopic dermatitis: Fine mapping and haplotype analysis. Ann Allergy, Asthma Immunol 125 (3): 287–293. doi: 10.1016/j.anai.2020.04.023.
20. Margolis L, Esch GW, Holmes JC, Kuris AM and Schad GA. The use of ecological terms in parasitology (Report of an adhoc committee of the American Society of Parasitologists). J. Parasitol. 1982; 68(1): 131-133.
21. Ozdamar M, Turkoglu S (2020) A nosocomial scabies outbreak originating from immunocompromised transplant patients in Turkey: Upholstery as a possible cause. Transpl Infect Dis 22 (4): e13284. doi: 10.1111/tid.13284.
22. Barwari WJ omer (2016) prevalence of scabies among refugees in camps of duhok province, kurdistan region, Iraq. Duhok Med J 10 (2): 109–116.
23. Hassan A, Mero W (2020) Prevalence of intestinal parasites among displaced people living in displacement camps in Duhok Province/Iraq. Internet J Microbiol, 17(1).
24. Liu JM, Wang HW, Chang FW, Liu YP, Chiu FH, Lin YC, et al (2016) The effects of climate factors on scabies. A 14-year population-based study in Taiwan. Parasite. doi: 10.1051/parasite/2016065
25. Welch E, Romani L, Whitfeld MJ (2021) Recent advances in understanding and treating scabies. Fac Rev 10
26. Korycińska J, Dzika E, Kloch M (2020) Epidemiology of scabies in relation to socio-economic and selected climatic factors in North-East Poland. Ann Agric Environ Med 27 (3): 374–378. doi: 10.26444/aaem/109319.
27. Mohy AA, Al-Hadraawy SK, Aljanaby AAJ (2018) Epidemiological study of patients infected with scabies caused by Sarcoptes scabiei in Al-Najaf Governorate, Iraq. Biomed Res 29 (12): 2650–2654. doi: 10.4066/biomedicalresearch.29-18-652.
28. Buczek A, Pabis B, Bartosik K, Stanislawek IM, Salata M, Pabis A (2006) Epidemiological Study of Scabies in Different Environmental Conditions in Central Poland. Ann Epidemiol 16 (6): 423–428. doi: 10.1016/j.annepidem.2005.06.058.
29. Walton SF (2010) The immunology of susceptibility and resistance to scabies. Parasite Immunol 32 (8): 532–540. doi: 10.1111/j.1365-3024.2010.01218.x.
30. Salah Hegab D, Mahfouz Kato A, Ali Kabbash I, Maged Dabish G (2015) Scabies among primary schoolchildren in Egypt: Sociomedical environmental study in Kafr El-Sheikh administrative area. Clin Cosmet Investig Dermatol 8 105–111. doi: 10.2147/CCID.S78287.
31. Walker SL, Lebas E, De Sario V, Deyasso Z, Doni SN, Marks M, et al (2017) The prevalence and association with health-related quality of life of tungiasis and scabies in schoolchildren in southern Ethiopia. PLoS Negl Trop Dis 11 (8): e0005808. doi: 10.1371/journal.pntd.0005808.
32. Nazari M, Azizi A (2014) Epidemiological Pattern of Scabies and Its Social Determinant Factors in West of Iran. Health (Irvine Calif) 06 (15): 1972–1977. doi: 10.4236/health.2014.615231.
33. Romani L, Steer AC, Whitfeld MJ, Kaldor JM (2015) Prevalence of scabies and impetigo worldwide: A systematic review. Lancet Infect Dis 15 (8): 960–967. doi: 10.1016/S1473-3099(15)00132-2.
34. Abdel-Aal AA, Hassan MA, Gawdat HI, Ali MA, Barakat M (2016) Immunomodulatory impression of anti and pro-inflammatory cytokines in relation to humoral immunity in human scabies. Int J Immunopathol Pharmacol 29 (2): 188–194. doi: 10.1177/0394632015627464.
35. Arlian LG, Morgan MS, Paul CC (2014) Evidence that scabies mites (Acari: Sarcoptidae) influence production of interleukin-10 and the function of T-regulatory cells (Tr1) in humans. J Med Entomol 43 (2): 283–287.
36. Mohammad ZAA, Hadi NA, Kawen AA (2020) Immunological aspects of patients infested with scabies in Thi-qar province, southern Iraq. Medico-Legal Updat 20 (3): 752–756. doi: 10.37506/mlu.v20i3.1607.
37. Bieber T (2020) Interleukin-13: Targeting an underestimated cytokine in atopic dermatitis. Allergy Eur J Allergy Clin Immunol 75 (1): 54–62. doi: 10.1111/all.13954.
38. Bin Huraib G, Al Harthi F, Arfin M, Al-Sugheyr M, Rizvi S, Al-Asmari A (2018) Cytokine Gene Polymorphisms in Saudi Patients With Atopic Dermatitis: A Case-Control Study. Biomark Insights 13 1177271918777760. doi: 10.1177/1177271918777760.
39. Reich K, Westphal G, König IR, Mössner R, Schupp P, Gutgesell C, et al (2003) Cytokine gene polymorphisms in atopic dermatitis. Br J Dermatol 148 (6): 1237–1241. doi: 10.1046/j.1365-2133.2003.05307.x.
40. Mallon E, Bunce M, Savoie H, Rowe A, Newson R, Gotch F, Bunker CB (2000) HLA-C and guttate psoriasis. Br J Dermatol 143 (6): 1177–1182. doi: 10.1046/j.1365-2133.2000.03885.x.
41. Kingo K, Kõks S, Silm H, Vasar E (2003) IL-10 promoter polymorphisms influence disease severity and course in psoriasis. Genes Immun 4 (6): 455–457. doi: 10.1038/sj.gene.6364004.
42. Miyake Y, Kiyohara C, Koyanagi M, Fujimoto T, Shirasawa S, Tanaka K, et al (2011) Case-control study of eczema associated with IL13 genetic polymorphisms in Japanese children. Int Arch Allergy Immunol 154 (4): 328–335. doi: 10.1159/000321825.
43. Lesiak A, Kuna P, Zakrzewski M, van Geel M, Bladergroen RS, Przybylowska K, et al (2011) Combined occurrence of filaggrin mutations and IL-10 or IL-13 polymorphisms predisposes to atopic dermatitis. Exp Dermatol 20 (6): 491–495. doi: 10.1111/j.1600-0625.2010.01243.x.
44. Hummelshoj T, Bodtger U, Datta P, Malling HJ, Oturai A, Poulsen LK, et al (2003) Association between an interleukin-13 promoter polymorphism and atopy. Eur J Immunogenet 30 (5): 355–359.

doi: 10.1046/j.1365-2370.2003.00416.x.
45. Lesiak A, Zakrzewski M, Przybyłowska K, Rogowski-Tylman M, Wozniacka A, Narbutt J (2014) Atopic dermatitis patients carrying G allele in -1082 G/A IL-10 polymorphism are predisposed to higher serum concentration of IL-10. Arch Med Sci 10 (6): 1239–1243. doi: 10.5114/aoms.2014.47833.
46. Rad R, Dossumbekova A, Neu B, Lang R, Bauer S, Saur D, et al (2004) Cytokine gene polymorphisms influence mucosal cytokine expression, gastric inflammation, and host specific colonisation during Helicobacter pylori infection. Gut 53 (8): 1082–1089. doi: 10.1136/gut.2003.029736.
47. Napolitano M, di Vico F, Ruggiero A, Fabbrocini G, Patruno C (2023) The hidden sentinel of the skin: An overview on the role of interleukin-13 in atopic dermatitis. Front Med 10 1165098. doi: 10.3389/fmed.2023.1165098.