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# ROLE OF IMMUNOCHEMICAL MEDIATORS IN ATOPIC DERMATITIS AND PARASITIC INFECTION

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## ABSTRACT

*Background* : Atopic dermatitis (AD) is an inflammatory skin disease that constitutes a significant burden to patients and their families. Parasitic infections as well are a cause of extensive morbidity in most tropical countries. Eosinophils are the predominant cells involved in these conditions. Upon activation of eosinophils by T helper 2 (Th-2) cytokines and their own mediators, they release granule proteins which can kill parasites and mediate inflammation in AD. *Aim*: the present study aimed to assess serum IgE and ECP and interleukines (IL-5 and IL-13) expression in atopic dermatitis and parasitic infection and their relation to disease activity. *Subjects and methods*: the present work was conducted on 45 patients, classified into group I: AD

(15 patients), group II: parasitic infection (Ascraisis and Schistomiasis) comprised 15 patients and group III: parasitic infection associated with allergic skin disease. In addition, 15 healthy subjects of matched age and sex were enrolled as a reference group. *Results*: Serum ECP and IgE levels were significantly elevated in all studied patient groups compared to the control and in group II and III compared to group I while insignificant difference was noted between group II and III. Eosinophil percent was significantly elevated in all patient groups compared to controls, but insignificant difference was found between patient groups. Moreover, serum IgE, ECP and eosinophil percent were significantly elevated in severe AD subgroup compared to moderate AD cases. Non significant correlation was

found between eosinophilic count and ECP while significant correlation was noted between ECP and severity of AD. The expression of IL-5 was evident in patients with parasitic infection with allergic manifestation 80% and in parasitic infection 46.6% and in atopic dermatitis 66.6% while IL-13 was evident in 86.6% of parasitic associated with allergy followed by parasitic 60% then atopic dermatitis 53.3%. Conclusion: Parasitic infection and atopic dermatitis are associated with intense Th-2 and eosinophilic activities resulting in increased IL-5 and IL-13 expression leading to elevation of ECP that mediates disintegration of parasites and inflammation in AD.

## INTRODUCTION

Atopic dermatitis is a common inflammatory skin disease with increasing prevalence, it interferes with nearly all aspects of daily life of the affected individual(1). Parasitic infection as well remains a major cause of morbidity and mortality world wide(2).

Atopic immune system is a component of the immune response regulated by a subset of T-cells termed T helper 2 (Th-2) cells and a series of cytokines creating inflammation mainly eosinophilic inflammation(3). Eosin-

ophilia and elevated IgE levels in parasitic infection and allergic diseases may represent two sides of the same coin. It is protective and beneficial in helminthic infestation while being detrimental to tissues in allergic disorders(2).

Eosinophil is a pro-inflammatory cell acts in a cellular network modulating the immune response(4). It acts through the release of granule proteins and the synthesis and release of inflammatory mediators. Eosinophilic cationic protein (ECP) is one of the cytotoxic performed mediators stored in eosinophil granules and released under various stimulations(5) such as interleukin-5 (IL-5)(6). ECP is a member of ribonuclease gene family and has a marked toxicity to a variety of helminthes parasites, bacteria, mammalian cells and tissues(7).

Delayed apoptosis of peripheral blood eosinophil in patients with atopic dermatitis was demonstrated and attributed to an increased autocrine production of granulocytes-macrophage colony stimulating factor (GM-CSF) and IL-5(8).

IL-13 is an immune regulatory and effector cytokine in allergic disease.

It is suggested to be a key cytokine in the pathogenesis of allergy<sup>(9)</sup>. IL-13 induces B-cell IgE production by isotype switching<sup>(10)</sup>. It is produced by T helper 2 (Th-2) cells however, eosinophil can produce IL-13 under inflammatory conditions such as atopic dermatitis and parasitic infection<sup>(11)</sup>.

The aim of this work was to assess serum ECP and total IgE levels and cytokine expression (IL-5 and IL-13) in atopic dermatitis and parasitic infection and their relation to disease activity in AD.

## SUBJECTS AND METHODS

The present study was conducted on 45 patients selected from Dermatology Department Tanta University Hospitals.

*They were classified into :*

**Group I:** Atopic dermatitis (15 patients) without parasitic infestation, they were diagnosed according to Hanifin and Rajki criteria<sup>(12)</sup>. Their age ranged from 4-21 years with a mean  $14.3 \pm 5.1$  years.

**Group II :** Parasitic infestation (15 patients) (schistosomiasis and ascariasis). Their age ranged from 5-20 years with a mean of  $15.6 \pm 7.6$  years.

**Group III :** Parasitic infestation as-

sociated with allergic skin manifestation (15 patients). Their age ranged from 5-30 with a mean of  $17.8 \pm 5.3$  years.

In addition, 15 healthy subjects with matched age and sex served as a control group.

None of the patients was undergoing any systemic therapy for a month prior to the study and all the subjects were free from other infections. Atopic dermatitis patients were affected by an exacerbation of chronic dermatitis. They were graded as moderate and severe according to the extent of skin lesion as assessed by William's<sup>(13)</sup> as follows:

- Mild cases: involvement of skin lesions up to 10% of body surface areas.
- Moderate cases : involvement of 10-70% of the body surface areas.
- Severe cases: involvement of more than 70% of the body surface area.

An informed consent was obtained from both patients and controls.

All patients and control groups were subjected to the following

- I) Complete history taking.
- II) Complete physical and dermatological examination.

## III) Laboratory investigations:

Helmenthic infection was diagnosed by stool analysis using Teleman technique.

*Sample collection :*

Venous blood samples were withdrawn from patients and controls under complete aseptic condition of which :

- One ml into EDTA tube for CBC using automatic blood count analyzer (Tecni-con H, Technicon. Tarrylown, NY).
- Three ml were withdrawn into plain tubes and non haemolysed sera were separated and used for:
  - Detection of schistosomiasis antibodies by indirect hemagglutination method<sup>(14)</sup> using Laboratoires Fumouze Kit (France).
  - Eosinophil cationic protein (ECP) using chemiluminescent enzyme immunometric assay by Immulite Automated Analyzer supplied by Diagnostic Product Corporation (USA)<sup>(15)</sup>.
  - Immunoglobulin E (IgE) determination by ELISA technique using commercially available kit from Omega Diagnostics Limited<sup>(16)</sup>.
- Five ml blood withdrawn into heparinized tube for the separation of peripheral blood mononuclear cells

(PBMC) for detection of interleukin expression. IL-5<sup>(17)</sup> and IL-13 expression<sup>(18)</sup> using RT-PCR.

*Extraction of RNA from PBMC :*

Mononuclear cells were isolated from heparinized venous blood by centrifugation over Ficoll-Hypaque according to Boyum<sup>(19)</sup>. They were immediately homogenized in isogen (Nippon Gene, Toyama, Japan) that contained phenol and acid guanidinium thiocyanate. Total RNA was isolated by QIAamp RNA extraction kit supplied by Qiagene (Germany).

*RT-PCR :*

Total RNA (50 ng) of each sample was reverse-transcribed using 2.5  $\mu$ M random hexamer, 5 mM  $MgCl_2$ , 50mM KCl. 10 mM Tris HCl pH 8.3, 1mM of each deoxynucleotide triphosphate (dNTP), 1.0U/ $\mu$ l RNasin (Takara, Tokyo, Japan), and 5 U/ $\mu$ l MMLV reverse transcriptase (GIBCO-BRL, Gaithersburg, MD). The mixture was pre-incubated at room temperature for 15 min., followed by incubation at 42°C for 45 min., at 99°C for 5 min., and finally at 5°C for 10 min. The resultant cDNA was amplified by PCR in a thermal cycler (Biometra uno II) with a final volume of 50  $\mu$ l

containing, 2mM Mg Cl<sub>2</sub>, 50mM KCl, 10mM Tris-HCl pH 8.3, 4U recombinant Taq DNA polymerase (Amersham pharmacia biotech), 5 ul of 200 umol/L of dNTPs and 25 pmol of forward and reverse primer. The oligonucleotide primers for PCR were based on published sequences(17,18).

The primer of IL-13 used was 5'CCTCAATC-CTCTCCTGTTGG-3' for the upstream primer and 5-TTTGGTGT-CTCGGACATGC-3' for the downstream primer.

The primer of IL-5 used was 5'-GAGCACAGTGG-TGAAAGAGACCTT-3' (upstream) and 5'-ATGACAGGTTTTGG-AATAGCATT-3' (downstream).

$\beta$ -actin was amplified to evaluate template integrity and efficiency of cDNA synthesis on a Biometra uno II thermal cycler using primer (forward-5'-GGC ATC GTG ATG GAC TCC G-3' and reverse-5'-GCT GGA AGO TGG ACA GCG A-3') was amplified for 28 cycles.  $\beta$ -actin PCR reactions were performed in 50-uL volume by

using 4 uL of 25 mmol/L MgCl<sub>2</sub>, 5 uL of 10x buffer, 5 uL of 200 umol/L of dNTP, 0.15 ug of  $\beta$ -actin primers, and 5 units of Taq polymerase. PCR amplification of  $\beta$ -actin was carried out for one cycle of 94°C for 3 minutes followed by 28 cycles with denaturation at 94°C for 30 seconds, annealing at 60°C for 1 minute, and extension at 72°C for 30 seconds. Amplicons were separated on 2% agarose gels stained with ethidium bromide. Photography of gels were performed. IL-5-specific amplicons and IL-13-specific amplicons were normalized to  $\beta$ -actin PCR products from the same experiment.

*Statistical analysis* : was done using SPSS program version 10. Student t test was used for comparing means of quantitative data. Presons' correlation (r) was used for correlation coefficient p value of  $\leq 0.05$  was considered statistically significant.

## RESULTS

are shown in Table (1-6), figure (I) and photo (1-2).

Results: are shown in Table (1-6), figure (I) and photo (1-2).

Table (1): Demographic data of studied groups:

		Control	Group I AD	Group II Parasitic	Group III AID + Parasitic
Number		15	15	15	15
Age(years)	Range	(5-25)	(4-21)	(5-20)	(5-30)
	$\bar{X} \pm SD$	17.7 $\pm$ 3.2	14.3 $\pm$ 5.1	15.6 $\pm$ 7.6	17.8 $\pm$ 5.3
Sex (M/F)		8/7	11/4	7/8	13/2

Table (2): Peripheral blood total Leucocytic count and eosinophils percent in studied groups:

Parameter	Control n(15)	Group I n(15)	Group II n(15)	Group III n(15)
TLC k/ul				
$\bar{X} \pm SD$	6.4 $\pm$ 1.3	7.6 $\pm$ 2.8	7.3 $\pm$ 3.2	8.1 $\pm$ 2.1
P		>0.05	>0.05	<0.05*
Eosinophils %				
$\bar{X} \pm SD$	2 $\pm$ 1	10 $\pm$ 6	7 $\pm$ 4	8 $\pm$ 4
P		<0.005*	<0.001*	<0.001*
		P <sub>1</sub> >0.05	P <sub>2</sub> >0.05	P <sub>3</sub> >0.05

\* Significant

P between studied groups and control.

P<sub>1</sub> (GP I&II)

P<sub>2</sub> (GP II&III)

P<sub>3</sub> (GP I&III)

Table (3): Comparison of serum IgE level among studied groups:

Parameter		Control n(15)	Group I n(15)	Group II n(15)	Group III n(15)
IgE (IU/ml)	Rang	6.2-80.2	20-480	50-500	65.8-840
	$\bar{X} \pm SD$	37.82 $\pm$ 20.24	167.6 $\pm$ 100	245.7 $\pm$ 132.4	358.0 $\pm$ 239.4
	P		<0.0005*	<0.0005*	<0.0005*
			P <sub>1</sub> <0.05*	P <sub>2</sub> >0.05	P <sub>3</sub> <0.05*

\* Significant

P (control and studied groups).

P<sub>1</sub> (GP I&II)

P<sub>2</sub> (GP II&III)

P<sub>3</sub> (GP I&III)

Table (4): Statistical data of serum ECP among studied groups:

Parameter		Control n(15)	Group I n(15)	Group II n(15)	Group III n(15)
ECP* (ng/ml)	Rang	2.4-27.2	5-80	5.9-112	6.9-116.9
	$\bar{X} \pm SD$	10.65 ± 8.13	25.8 ± 15.77	40.22 ± 25.91	53.2 ± 31.2
	P		<0.01*	0.01*	<0.0005*
			P <sub>1</sub> <0.05*	P <sub>2</sub> >0.05	P <sub>3</sub> <0.02*

\* Significant

P (control and studied groups).

P1 (GP I&amp;II)

P2 (GP II&amp;III)

P3 (GP I&amp;III)

Table (5): Statistical data of studied parameters in severe versus moderate AD patients:

Parameter		moderate AD n(9)	Severe AD n(6)	P-value
ECP (ng/ml)	$\bar{X} \pm SD$	17.4 ± 10.7	33.9 ± 19.8	<0.05*
IgE (Iu/ml)	$\bar{X} \pm SD$	90.8 ± 40.5	247.6 ± 160.8	<0.05*
Eosinophil %	$\bar{X} \pm SD$	5 ± 4	15 ± 8	<0.05*

\* Significant

Table (6): Correlation coefficient between ECP, eosinophil % and severity of disease in atopic dermatitis.

Parameter		Eosinophil %	Severe of AD
ECP	r	0.2	0.67
	p	>0.05	<0.001
Eosinophil	r	-	0.3
	p	-	>0.05



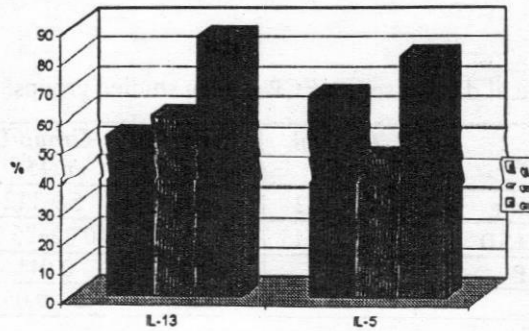


Figure (I) : percent of cases expressing IL-5 and IL-13 in studied groups.

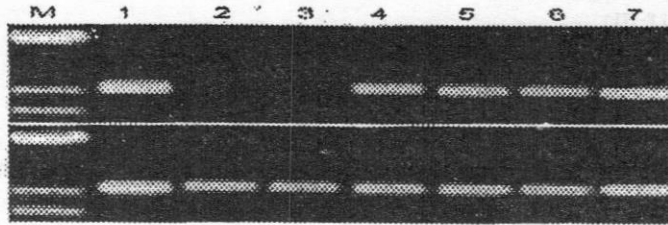


Photo (1) : RT-PCR of IL-5. PCR products (197 bp) in different patient groups compared to control group. Lane M: molecular marker of 100 bp ladder, Lane 1,4,5,6,7 show patients with positive IL-5 expression, Lane 2,3 show negative expression compared to  $\beta$ -actin in the lower column. The expression of IL-5 was evident in the patients complaining of both atopic dermatitis with parasitic infection (12 out of 15) 80%, (7 out of 15) 46.6% in patients complaining of parasitic alone and (10 out of 15) 66.6% in patients complaining of atopic dermatitis alone.

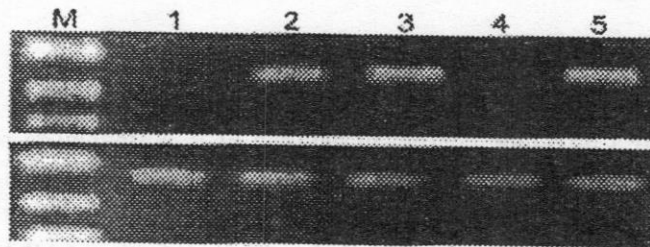


Photo (2) : RT-PCR of IL-13. PCR products (430 bp) were separated on 2% agarose gel and stained by ethidium bromide Lane M: molecular marker of 100 bp ladder, Lane 2,3,5 show patients with positive IL-13 expression, Lane 1,4 show negative expression compared to  $\beta$ -actin in the lower column. The expression of IL-13 were evident in the patients complaining of both atopic dermatitis with parasitic infection (13 out of 15) 86.6%, (9 out of 15) 60% in patients complaining of parasitic alone and (8 out of 15) 53.3% in patients with AD.

## DISCUSSION

Atopic dermatitis (AD) is a chronic inflammatory skin disease with a pathogenesis of complex immune dysregulation (*alteration of cellular and humoral immunity*) and interplay of genetic, environmental and psychological factors. Activation and skin-selective homing of peripheral-blood T cell, and effector functions in the skin, represent sequential immunological events in the pathogenesis of atopic dermatitis.(20)

Helminth parasites are a cause of extensive morbidity in most tropical countries(21). Eosinophils and their granule proteins are significant participant in the inflammatory process in allergic disease and in host parasite interaction. The present work aimed to assess the role of immunochemical mediators in AD and parasitic infection.

The present study revealed significant elevation of serum levels of ECP and IgE in the three studied group compared to the control group and in group II and III compared to group I. However, non significant difference was found between group II and III (Table 3, 4). Moreover, they were significantly elevated in severe com-

pared to moderate atopic dermatitis (Table 5).

Eosinophil percent was significantly elevated in the three studied groups compared to the control but insignificant difference was noted among the three studied groups (Table 2). In addition ECP is not correlated to eosinophil count, but correlated to severity of AD (Table 6).

AD and parasitic infections are characterized by blood and tissue eosinophilia. It was reported that serum concentrations of ECP appears to mirror the functional activity of the eosinophilic leukopocetic system in the particular host(22). Like other granule proteins, ECP mediates membrane damage and together with oxygen radicals are responsible for killing and disintegration of helminthes(23). Moreover, extensive extracellular dermal deposits of ECP has been reported to occur in eczematous skin lesion of AD. In addition, eosinophil activity in AD participate in patch test reactions (24).

In consistence to this finding, other investigators reported that ECP was elevated in serum of AD patients, and no correlation was found between

serum level of ECP and blood eosinophil count (neither in AD nor helminthics)(25).

It has been reported that eosinophilic proteins play a crucial role in host defense against helminthic parasites(2) as it is toxic to helminth parasites(7) and schistosoma mansoni(26).

In the present study, the lack of a positive correlation between ECP and peripheral blood eosinophils many indicate that serum granule proteins not only derived from peripheral blood cells but also from activated eosinophils in tissues. The level of ECP observed in helminthic diseases exceeded those found in atopic dermatitis this finding is in accord to previous study(2). In AD the level of ECP correlated with the grading of severity of clinical evaluation ( $r=0.67$ ,  $P<0.001$ ) (Table 6). Moreover, ECP was found to be more significantly elevated in AD patients with severe chronic exacerbation (6 out of 15 patients) than moderate (cases 9 out of 15 patients). This finding is in agreement with Kirn park et al.(27) who stated that ECP may be a helpful tool for monitoring disease activity in AD. However, Pescollderungg et al.(28) and Nieto (29)

reported that isolated ECP is probably of limited value due to large overlap of results between different conditions. Also, ECP mean value was more elevated in the patients with higher antibody titer to schistosomiasis ( $>1/640$ ) (3 out of 15 patients) than those with lower antibody titer ( $<1/320$ ) (12 out of 15 patients). It was reported that higher ECP level in chronic helminthic infection seem to reflect an augmented degree of antigenic stimulation, eosinophils activation and eosinophils turnover rates, indicating a more active mechanism of parasite clearance(30).

Regarding IgE, although there is some debate regarding the relationship between helminthic, IgE response and allergic states(31,32) there is considerable evidence that IgE antibody is an important component of immune protection against parasites(33,34). The hall mark of helminth infection in immunological term is elevated IgE and eosinophilia exceeding the level in atopic dermatitis and asthma(21). It has been well established that helminthic infections not only stimulate IgE response against their own antigen but also induce a strong non specific Th1/IL-4 dependent polyclonal synthesis of this im-

munoglobulin(35,36). The non specific synthesis of this polyclonal stimulation can suppress allergic responses by reducing the production of specific IgE-Ab against any given antigen and by causing mast cell blockage by FC epsilon receptor saturation(37,38). One consequence of this is a reduction of the allergic reactivity against environmental allergens in AD patients with helminthiasis(39). Perhaps of even greater importance is the possibility that the inhibitory effect of excess IgE represents a mean of evasion of the parasites from the immune response(40). In this respect, it was previously shown that in endemic areas, persons with the highest total IgE level are preferentially re-infected after anti-helminthic treatment(41).

On the other hand, other study reported that the prevalence of helminthic infection was lower in atopic individuals than in their non atopic counterpart in the same geographic area. Moreover, children with a strong atopic background demonstrated IgE response can cordant with an enhanced protective response against helminthic parasites and had significantly lower intensities of infection than their non atopic counterpart(42). These observations support the con-

cept that the atopic state has confined a selective evolutionary advantage that could compensate for its involvement in allergic disease(34).

There is overwhelming evidence that abnormal Th1/Th2 functions contribute not only to the production of IgE but also to the pathogenesis of allergic disorder(43).

Cytokine concentrations in the serum are often low to be measured by (ELISA) and the reported values obtained by ELISA vary considerably(44) so the present study assess IL-13, IL-5 expression using RT PCR.

In the present study there was increased expression of PBMC IL-13 and IL-5 mRNA in the patients with AD, patients with parasitic infection alone and combined AD with parasitic infection (53.3 %, 60% and 86%) and (66.6%, 46.6% and 80%) respectively (Figure 1). However, Farrell et al.(44) reported very low CD4+ and CD8+ T-cells expressing IL-5 in the peripheral blood of AD patients. So, the increased IL-5 expression in the present study may be due to auto-crine production of IL-5 from eosinophils(5). Since serum levels of IgE were elevated in most of the patients

expressing IL-13, this suggest that IL-13 may have played a role in the increased synthesis of IgE seen in these patients. These results agree with Katagiri et al;<sup>(45)</sup> who stated that IL-13 has the ability to promote IgE synthesis and is considered to be an important cytokine in atopic disease.

It is well known that Th-2 cells orchestrate allergic inflammation and provide help for humoral immune-response<sup>(46)</sup>. They play a crucial role in providing protection against multicellular parasites through production of IL-4, IL-5 and IL-13<sup>(2,42)</sup>. Moreover, IL-13 has been reported to be produced by eosinophil under certain inflammatory condition such as AD and parasitic infection. Eosinophil derived IL-13 is functional as it increases low affinity IgE receptor (CD33) on purified B-cells<sup>(11)</sup>. The increased expression of IL-13 and IL-5 leads to enhanced activity and prolonged survival of eosinophils which is responsible for elevated level of ECP<sup>(47)</sup>.

In the same way Th-2 play a key role in peripheral blood eosinophilia and eosinophil activation. Activated eosinophils release their granule proteins including ECP into the peripher-

al circulation or inflammatory skin lesions and subsequently provoke a clinical exacerbation of allergic reactions<sup>(39)</sup>. Also, activated eosinophils have high affinity IgE receptors (Fc ERI) which are involved in host defense against parasites<sup>(49)</sup>,

Finally, it could be concluded that there is a greater activity of eosinophil cell system in helmenthic disease and in AD and both diseases could affect the rational history of the other. Moreover IL-5 and IL-13 have important role in the pathogenesis of AD and host-parasite interaction and ECP is a valuable diagnostic tool in detecting the degree of eosinophil activation.

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## دور الوسائط المناعية الكيميائية فى حساسية الجلد والعدوى الطفيلية

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تعتبر حساسية الجلد والعدوى الطفيلية من الأمراض التى تمثل عبئاً مرضياً بالنسبة لكل من المرضى وذويهم وتلعب الخلايا الليمفاوية (المساعدة ت-٢) دوراً أساسياً فى هذه الأمراض خلال حث كلا من الخلايا الليمفاوية (ب) فى تكوين أجسام مناعية (E) وكذا الخلايا الأيوسنية وذلك بما تفرزه من وسائط مناعية مثل الانترلوكين ١٣.٥ التى تنشط الخلايا الأيوسنية وتعمل على إطالة عمرها وتقوم الخلايا الأيوسنية النشطة بافراز مخزنها من البروتينات الأيوسنية منها البروتين الكاتيونى الأيوسينى الذى يعمل على قتل الطفيليات وكذا يؤدى الى الالتهاب فى حساسية الجلد.

وقد هدفت هذه الدراسة الى تقييم الدور الذى تلعبه الوسائط المناعية (الانترلوكين ١٣.٥) والكيميائية (البروتين الأيوسينى الكاتيونى) فى مرضى حساسية الجلد والعدوى الطفيلية وعلاقتها بشدة المرض.

وقد اشملت هذه الدراسة على ٤٥ مريضاً فى ثلاث مجموعات :

مجموعة (١) : مرضى حساسية الجلد وتشمل ١٥ مريضاً.

مجموعة (٢) : مرضى العدوى الطفيلية (البلهارسيا والاسكارس) وتشمل ١٥ مريضاً

مجموعة (٣) : مرضى العدوى الطفيلية والمصابة بحساسية الجلد وتشمل ١٥ مريضاً

بالاضافة الى مجموعة من الأصحاء ١٥ شخصاً مماثلين فى الجنس والعمر بالنسبة للمرضى وقد تم

عمل الفحوصات الآتية لكلا من المرضى ومجموعة الأصحاء :

(١) صورة دم كاملة شاملة نسبة الخلايا الأيوسنية.

(٢) البروتين الكاتيوني الأيوسيني والأجسام المناعية (E)

(٣) الحامض النووي الرسول لكلا من الانتروكين ١٣.٥ بطريقة تفاعل سلسلة البلرمة

وقد أسفرت النتائج عن زيادة الأجسام المناعية (E) وكذا البروتين الأيوسيني الكاتيوني فى مجموعات المرضى عند مقارنتها بالأصحاء وزيادتها فى كلا من المجموعة الثانية والثالثة عند مقارنتها بالمجموعة الأولى. كما وجد زيادة فى نسبة الخلايا الأوسينية فى مجموعات المرضى الثالث عند مقارنتها بمجموعة الأصحاء ولا يوجد فرق ذو دلالة احصائية فيما بين المجموعات الثالث ووجدت علاقة ذات دلالة إحصائية بين شدة المرض والبروتين الأيوسيني الكاتيوني ولكنه لا توجد علاقة بين نسبة الخلايا الأيوسينية وشدة المرض. وجدت زيادة فى الخلايا الأيوسينية والأجسام المناعية والبروتين الأيوسيني فى المرضى ذوى الحساسية الشديدة عن مجموعة الحساسية المتوسطة

وجد أن الحامض النووي الرسول لكلا من النتروكين ١٣.٥ أكثر وضوحاً فى المجموعة الثالثة ٨٦.٦٪ تليها المجموعة الثانية ٤٦.٦. ٦٠٪ ثم المجموعة الأولى ٣٠.٦٠، ٥٣.٣٪.

مما سبق يمكن إستنتاج أن زيادة الحامض النووي الرسول لكل من الانتروكين ١٣.٥ فى كل من حساسية الجلد والعدوى الطفيلية والذى يؤدى الى زيادة نشاط الخلايا الليمفاوية (ب) فى إفراز الأجسام المناعية (E) وكذا نشاط الخلايا الأيوسينية التى تفرز بدورها البروتين الأيوسيني الكاتيوني الذى يؤدى الى قتل الطفيليات وحدوث الالتهاب فى حساسية الجلد.