Assessment of Serum Interleukin-4 and Filaggrin Protein in Patients with Atopic Dermatitis

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Abstract

The current study aimed to determine the relationship between certain immunological parameters inatopic dermatitis (AD) patients.

There wasno significant differences (P≥0.05)in the level offilaggrin protein between patients and control groups regarding to the age but there wasa significant differences (P≤ 0.05)in the level of IL-4 between patients and healthy subjects groups regarding to the age, also the study showed that there was no significant differences (P≥0.05) between study groups regarding the gender for above two parameters.

The data of current study support the defected skin barrier role in the AD pathogenesis, in addition the results revealedfilaggrin reduced expression in atopic skin lesion and inverse correlation between filaggrin protein expression and disease severity. Add to that, the elevation of circulation interleukin IL-4 levels in AD, emphasizes the profile of systemic inflammation of this skin barrier defective dermatosis.

Keywords: *IL-4; Filaggrin protein; Atopic dermatitis.*

Introduction

Atopic dermatitis (AD) is the most common chronic inflammatory skin disease[1]. It starts in early infant life and remains lifelong with therapeutic difficulty especially when it is in moderate or severe form[2]. Its etiology remains poorly understood but it is believed as multifactorial with complex combination of deviation in the immune system, defective barrier function and risk of environmental factors[3,4] leading to allergens skin sensitization as a result of mutations affecting the epidermalbarrier orbecause of an inflammation that inhibit the epidermal differentiation[5].

AD as a heterogeneous disease, activating more than one inflammatory pathway with psoriasis where IL-4 play an important role in the allergic response. IL-4 and IL-13 are involved in the promotion of isotype class switching from IgM to IgE that stimulate T cell differentiation to Th2 and B cells antigen presenting enhancement[6]. Filament aggregating protein (filaggrin) is important for cornified cell envelope (CCE) formation that is nedded for effective skin barrier where it binds to and facilitates keratins (K1/10) aggregation that induce the collapse of cytoskeletonto formcorneocytes[7].

Materials and Method

Patients and Control: The work was applied on 49 patients (23 males, 26 females) admitted to the Imam Sadiq Hospital & Merjan Hospital (Dermatology Advisory Unit) in Babylon Governorate and 30 healthy subjects (11 males, 20 females) without prior clinical signs as control group. All patients were initially diagnosed by specialist physician.

Blood Samples: The blood samples (5ml) were drawn from each patients and controlgroups by vein puncture using disposable syringes. The blood was placed in the Jell tube and kept to clot atroom temperature, then centrifuged at 3000 rpm for 10 min., after that, sera samples were carefully transferred to Eppendorf tubes and preserved at -20°C untiluse.

Immunological Tests: The levels of immunological criteria IL-4 and Filaggrin, were estimated by ELISA Kit according to the manual procedures of Elabscience (USA) and Biolabs (China) respectively.

Statistical Analysis: The results were analyzed using the ANOVA-LSD-General Linear Model and SPSS (copyright 16).

Results

The results of present study (table 1),showed no significant differences (P≥0.05)in the Filaggrinprotein level between patient and control groups regarding to the age, also the study shown increase the concentration of this parameter in age category≤ 20 years,whilethe low of its level represented in age category (≥60) years as revealed in figure (1). Whereas the results for IL-4 cytokine was show a significant differences (P≤ 0.05) between patients and controls regarding to the age; and the study shown increases the concentration of IL-4 in age category(41-60) years, while alow concentration was demonstrated in the age group ≥ 60 years Figure (1). Regarding to the gender the results in table (2) and figure (2) were showed no significant differences (P≥0.05) between patients and controls in the levels offilaggrin protein and IL-4.

Table 1: The levels of filaggrin protein and IL-4 in patients with atopic dermatitis according to the age groups.

Groups	Age (Year)	NO.	Filaggrin protein (ng) Mean±S.E	IL-4 (Pg/ml) Mean±S.E
Control	≤20	13	4.58±4.13	273.11±100.5
	21-40	7	2.94±3.57	148.30±90.51
	41-60	9	2.28±1.17	273.07±99.63
	≥60	2	1.32±0.41	131.67±73.07
Patients	≤20	14	3.33±1.12	66.50±29.23
	21-40	23	3.09±1.15	77.72±24.22
	41-60	11	2.81±0.74	79.70±26.50
	≥60	1	1.44±0.0	58.09±0.0
$LSD_{(0.05)}$			N.S	25.123

Table 2: The levels of filaggrin protein and IL-4 in patients with atopic dermatitis according to the gender.

Groups	Gender	Filaggrin protein (ng) Mean±S.E.	IL-4 (Pg/ml) Mean±S.E.
Control	Male (n.11)	4.18±1.26	129.00±25.54
	Female (n.20)	2.86±0.62	294.52±59.19
Patients	Male (n.23)	3.42±0.84	65.42±5.17
	Female (n.26)	2.74±0.60	82.64±19.47
$LSD_{(0.05)}$		2.471	105.41

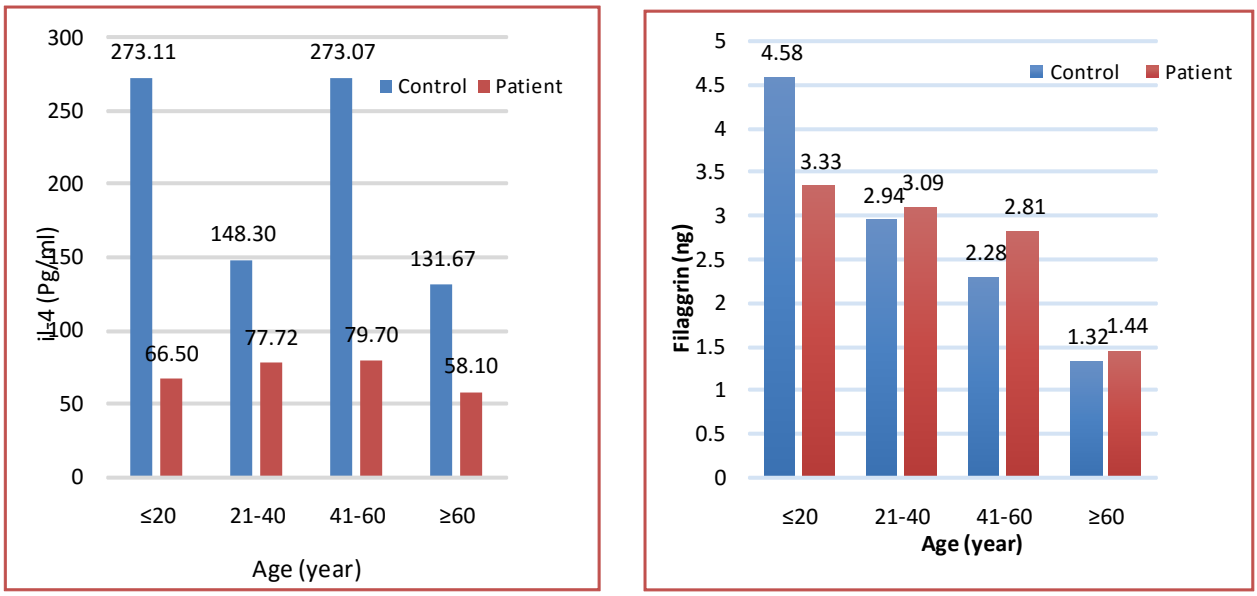

Figure 1: The levels of filaggrin protein and IL-4 in patients with atopic dermatitis according to the age groups

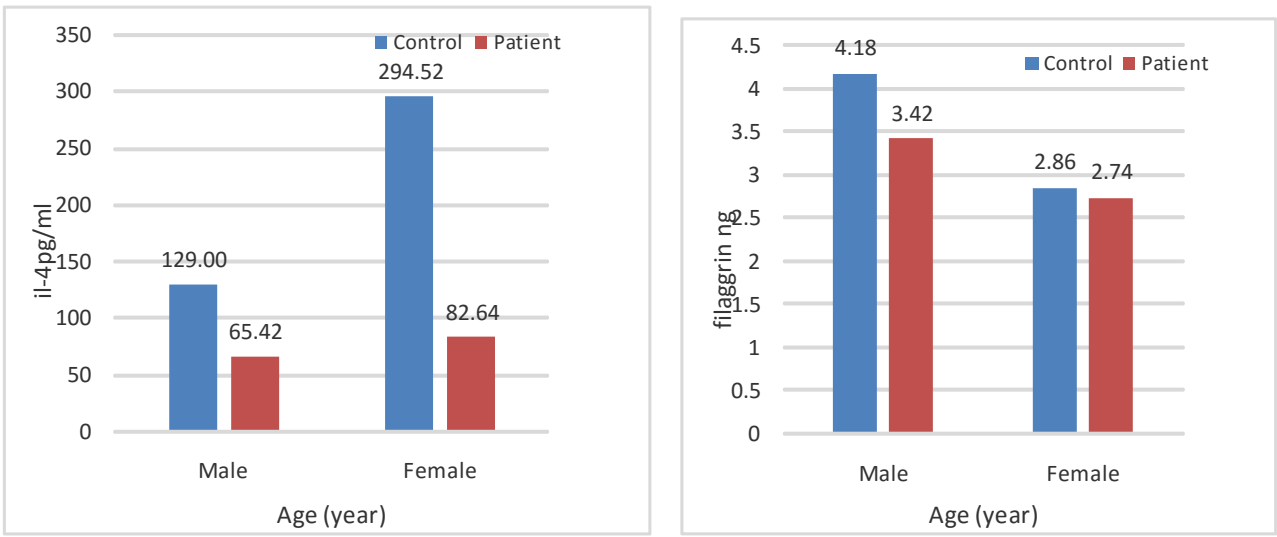

Figure 2: The levels of filaggrin protein and IL-4 in patients with atopic dermatitis according to the gender

Discussion

The results of immunological criteria showed that there were no significant differences ($P \geq 0.05$) in the concentration of filaggrin protein and the correlation analysis showed no correlation significant between age and gender for atopic groups compared with controls.

Filaggrin protein: Acute AD skin is associated with Th2 cytokines over expression (IL-4 and IL-13), combined with increased filaggrin expression. Therefore, whether these cytokines alter the filaggrin expression was investigated.

The current study indicated that this deficiency is partially due to the Th2 cytokines over expression that inhibit filaggrin expression that agree with[8].

Further studies need to be conducted to determine whether the early AD treatment may repair skin barrier defect. There is an association between filaggrin gene mutationand AD[9].

Interleukin-4(IL-4): The results revealed a significant difference ($P \leq 0.05$) and also a significant correlation with age between atopic and control groups.

The present studyagree with[10] who indicated that acute skin lesions contain more cells that produce IL-4, IL-5 and IL-13, but not IFN-ɣin comparison with chronic lesions where IL-4 and IL-13 are significantly decreased and increased cells expressing IL-5 and IFN- ɣ[11]

IL-4 Overexpression in the epidermis, developed all marks of AD like increased inflammatory cells in the skin,pruritus, skin bacterial infection and increased IgG1 and IgE [12].

The results of this study disagree with[13]reported that the Th2 cells are responsible for the development of the humoral immune response and the hyperproduction of IL-4, IL-10, IL-13 in allergic diseases.

Another study showed high serum levels of cytokines in the eczematous lesions patients either acuteor chronic,due to increased Th2 cells secreting IL-4 and IL-13, while high TNF serum levels in chronic lesions[14].

The current study agree with the results of [15] whom observed higher levels of IL-4, IL-13 and IFN-γ in chronic eczema.

Conclusion

The data of current study support the defected skin barrier role in the AD pathogenesis, in addition the results revealed filaggrin reduced expression in atopic skin lesion and inverse correlation between filaggrin protein expression and disease severity. Add to that, the elevation of circulation interleukin IL-4 levels in AD, emphasizes the profile of systemic inflammation of this skin barrier defective dermatosis.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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