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Original Article

Evaluation of Serum Periostin Level and Its Association with Disease Severity and Chronicity in Paediatric and Adult Patients with Atopic Dermatitis: A Case-Control Study

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Abstract

Background: Atopic Dermatitis (AD) affects both children and adults. Periostin is highly expressed in the dermis of lesions in AD patients.

Aims and Objectives: The present case-control study aimed to evaluate serum periostin level and its association with disease severity and chronicity in paediatric and adult patients with AD as compared with healthy controls.

Materials and Methods: The study included 74 children (53 AD patients [38 males] and 21 controls [12 males]) and 70 adults (40 AD patients [27 males] and 30 controls [13 males]). Disease severity was evaluated using the SCO Ring Atopic Dermatitis (SCORAD) index. Chi-square and Mann-Whitney U tests and Spearman's correlation analysis were used.

Results: The mean periostin level was significantly higher in the paediatric patients than in the paediatric controls (70.5±48.1 ng/mL *vs*. 69.8±62.7 ng/mL; p=0.025) but did not differ between the adult patients and adult controls (74.9±53.3 ng/mL *vs*. 86.3±79.6 ng/mL, p=0.235). It was significantly higher in males than in females in the adult group (p=0.014) and was similar between the patients with and without an allergic disease in both groups. Spearman's correlation analyses revealed no association of periostin level with disease severity and disease chronicity in both groups but showed a significant positive correlation of the SCORAD index score with disease duration (r=0.359, p=0.010) and with total immunoglobulin E level (r<0.001, p<0.001) in the paediatric group.

Conclusion: In the study, an association between periostin level and AD was suggested particularly in paediatric patients. Periostin level in AD should be evaluated in further studies including larger samples having diverse backgrounds.

Keywords: Periostin; Atopic dermatitis; Children; Adults; SCORAD index

Introduction

Atopic Dermatitis (AD) is a chronic and inflammatory skin disease, which affects both children and adults [1]. The current estimates about the epidemiological characteristics of childhood AD has revealed that the prevalence of the disease is higher in developed and wealthier nations than in the poorer and developing countries [2,3]. The literature data have also suggested a significant distribution pattern all over the world that ranged between 0.9% in India to 22.5% in Ecuador for children at 6 to 7 years of age and 0.2% in China to 24.6% in Colombia for children at 13 to 14 years of age [4]. For the adult type AD, the prevalence estimates range between 2.0% to 6.9%.5, 6 Based on the currently available evidence about the epidemiology of AD, the prevalence seems to be at the highest level in childhood (13-14 %), decreased through adolescence (8%), and remains stable in adulthood (6-8 %) [7].

Atopic dermatitis is clinically characterized as a skin disease with multifaceted, chronic, relapsing and inflammatory properties, which are commonly associated with several other atopic presentations including allergic rhinitis, food allergy, or asthma [8,9]. There are two significant established risk factors for AD progression, which are genetic defects in the FLG gene and the presence of family history of AD [10,11]. The FLG gene is responsible for the expression of profilaggrin protein, which is found in the granular layer of the epidermis and plays a role in adherence of structural proteins to form a strong barrier matrix [12]. Mutations in this gene results in deterioration and dysfunctions in the skin barrier [13,14]. Moreover, patients with AD have a genetically determined dominance of T-helper 2 (Th2) cells, which may decrease the expression of FLG gene and other molecules in the skin barrier [8]. Genetically engineered mice overexpressing Th2 cells have been shown to have spontaneous progression of AD [15].

Periostin is an extracellular matrix protein (an N-glycoprotein) that belongs to the fasciclin family and is secreted predominantly by the dermal fibroblasts. Periostin binds to other extracellular matrix

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components to maintain the structure of the dermis [16]. While periostin is found mainly in the papillary dermis and in the basement membrane of the epidermis in the normal skin, it is highly expressed in the dermis of the lesions in patients with AD. Periostin has been found to induce Th2-type cytokines such as Interleukin (IL)-4 and IL-13 and chemokines such as Thymic Stromal Lymphopoietin (TSLP), which has a role in amplification and chronicity of allergic skin inflammation [17].

The aim of the present study was to evaluate the periostin levels in paediatric and adult patients with AD and to compare these levels with that of healthy controls. Moreover, the association between severity of AD and periostin levels was also evaluated for paediatric and adult patients separately.

Materials and Methods

The present study included a total of 53 paediatric patients and 40 adult patients with AD who were diagnosed, treated, and followed-up in the Dermatology Department of Istanbul University Cerrahpasa Medical Faculty between May 2019 and December 2019. A control group was also formed from volunteer healthy individuals (from children or adults according to the group) having no dermatological diseases both for the paediatric and adult groups. The diagnosis of AD was established based on the Hanifin and Rajka criteria and the disease severity was evaluated using the SCORing Atopic Dermatitis (SCORAD) index [18]. The present study was approved by the Clinical Research Ethics Committee of XXX Medical Faculty (approval number: 39122051-604.01.02-44210; dated March 19, 2019) and informed consents were obtained from the patients and/or their legal guardians. The procedures followed were in accordance with the ethical standards of the responsible committee and with the Helsinki Declaration of 1975, as revised in 1983.

Serum levels of periostin were analysed using human periostin ELISA kit (Bioassay Technology Laboratory, Shanghai, China) according to the manufacturer's instructions. Biochemical analyses for eosinophil counts and total immunoglobulin (Ig) E levels were performed in the Biochemistry Department of Istanbul University Cerrahpasa Medical Faculty. Age at disease onset, disease duration, and presence/absence of allergic disease were also evaluated as study parameters.

Statistical analyses

Data analyses were performed using the IBM SPSS Statistics for Windows version 21.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics were expressed as mean and standard deviation for numerical variables and as frequency and percentage for categorical variables. The comparisons between independent groups were performed using the Chi-square test and the Mann-Whitney U test for categorical and numerical variables, respectively. Spearman's correlation analysis was performed for evaluating the association of periostin levels and SCORAD index score with other study parameters. A type-I error level of 5% was used to detect statistical significance in hypothesis testing.

Results

The present study included 53 paediatric patients (M/F: 38/15) and 21 paediatric controls (M/F: 12/9) as the paediatric group and 40 adult patients (M/F: 27/13) and 30 adult controls (M/F: 13/17) as the adult group. The distribution of males and females was similar in the paediatric patients and controls (p=0.23); however, there was a female predominance in the controls as compared with the patients for the adult group (p=0.043). General features, disease parameters, and clinical characteristics of the patients and controls are summarized in (Table 1).

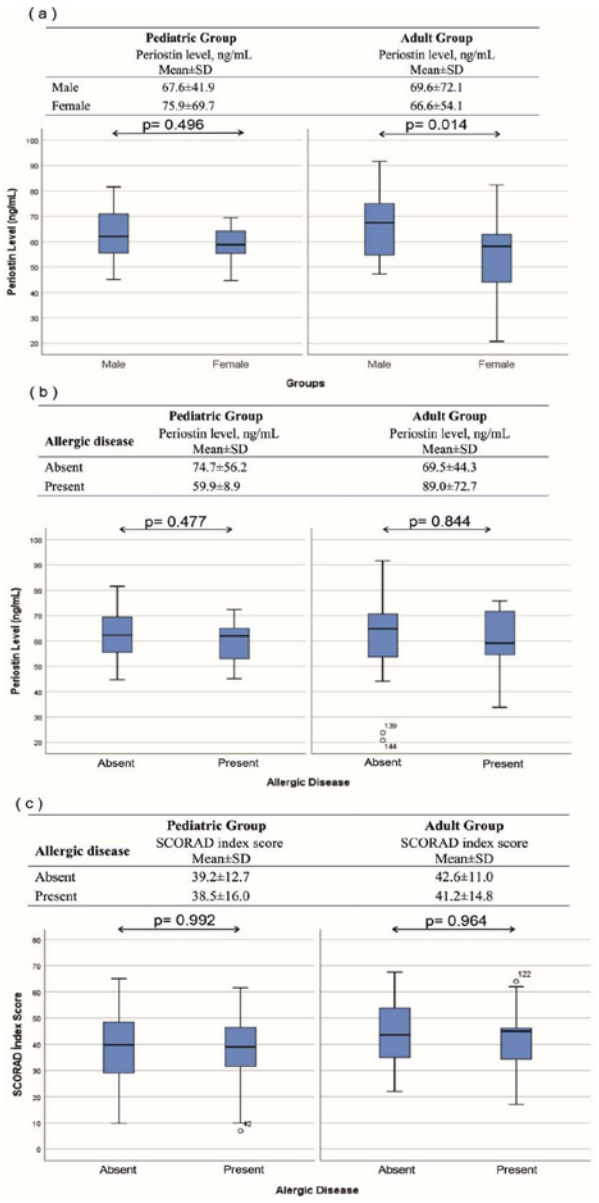

Figure 1: Comparisons of periostin levels according to (a) sex and (b) presence of an allergic disease and (c) comparison of SCORing Atopic Dermatitis (SCORAD) index scores regarding presence of an allergic disease in the pediatric and adult patient groups. SD, standard deviation.

The comparison of the periostin levels revealed that while the paediatric patients had significantly higher periostin levels as compared with the paediatric controls (p=0.025), there was no significant difference between the adult patients and adult controls in terms of periostin levels (p=0.235) (Table 1). The comparisons of

Table 1: General features, disease parameters, and clinical characteristics of the patients and controls in the pediatric and adult groups.

	Pediatric Group (n=74)			Adult Group (n=70)		
Characteristics	**Patients (n=53)**	**Controls (n=21)**	**p**	**Patients (n=40)**	**Controls (n=30)**	**p**
Age, years, Mean±SD	9.4±6.7	12.0±5.0	0.012	35.9±13.5	36.9±9.5	0.498
Sex, n (%)			0.23			0.043
Male	38 (71.7)	12 (57.1)	0.23	27 (67.5)	13 (43.3)	0.043
Female	15 (28.3)	9 (42.9)		13 (32.5)	17 (56.7)	
Allergic disease, n (%)						
Absent	38 (71.7)	-		29 (72.5)	-	
Present	15 (28.3)	-		11 (27.5)	-	
Age at disease onset, years, Mean±SD	5.0±6.2	-		21.7±17.1	-	
Disease duration, years, Mean±SD	4.5±3.6	-		14.5±14.4	-	
SCORAD score, Mean±SD	39.0±13.6	-		42.2±12.0	-	
Eosinophil ratio, Mean±SD	5.1±5.3	-		6.6±6.3	-	
Eosinophil count, K/μL, Mean±SD	0.9±1.4	-		0.7±1.0	-	
Total IgE, kU/L, Mean±SD	897.1±2181.5	-		1899.3±4276.0	-	
Periostin level, ng/mL, Mean±SD	70.5±48.1	69.8±62.7	0.025	74.9±53.3	86.3±79.6	0.235

SD: Standard Deviation; SCORAD: SCORing Atopic Dermatitis; IgE: Immunoglobulin E

periostin levels according to sex and presence of an allergic disease and the comparisons of SCORAD index scores according to presence of an allergic disease both in the paediatric and adult patients are shown in (Figure 1). Accordingly, while the mean periostin level was found to be significantly higher in males in the adult patient group (p=0.014), it was higher in females in the paediatric patient group but the difference was not statistically significant (p=0.496).

The Spearman's correlation analyses performed to evaluate the association between periostin levels and other study parameters demonstrated that none of the study parameters (age, age at disease onset, disease duration, the SCORAD index scores, eosinophil ratio and count, and total IgE levels) were correlated with periostin level either in the paediatric or in the adult group (Table 2). The periostin levels were also similar between the patients with and without an allergic disease both in the paediatric patient group (p=0.477) and in the adult patient group (p=0.844) (Figure 1).

The Spearman's correlation analyses performed to evaluate the association of disease severity measured by the SCORAD index scores with disease duration and total Ig E levels demonstrated that there was a significant positive and weak correlation between the SCORAD index score and the disease duration (r=0.359, p=0.010) and a significant, positive and moderate correlation between the SCORAD index score and total Ig E level (r<0.001, p<0.001) in the paediatric patient group (Table 2). On the other hand, the SCORAD index score was not found to be correlated with disease duration and total IgE level in the adult patient group (Table 2). There were also no significant differences in the SCORAD index scores of patients with and without allergic diseases both in the paediatric patient group (p=0.992) and in the adult patient group (p=0.964) (Figure 1).

Table 2: Results of correlations of periostin levels and SCORAD index scores with other study parameters in the pediatric and adult groups.

	Pediatric Group			Adult Group	
	r	**p**		**r**	**p**
Periostin level					
Age	-0.013	0.927		0.08	0.624
Age at disease onset	0.116	0.41		-0.295	0.065
Disease duration	-0.115	0.422		0.262	0.103
SCORAD index score	0.058	0.677		0.172	0.289
Eosinophil ratio	0.042	0.768		0.242	0.138
Eosinophil count	-0.123	0.391		0.21	0.205
Total IgE	-0.024	0.866		0.03	0.855
SCORAD index score					
Disease duration	0.359	0.01		-0.15	0.357
Total IgE	0.556	<0.001		0.292	0.068

Discussion

The present study evaluated the periostin levels in AD for paediatric and adult patients. The periostin levels were determined to be significantly increased in paediatric patients as compared with paediatric controls but were not found to be associated with the parameters evaluated in the study. In adults, no association was found between periostin levels and presence of AD; however, males were observed to have significantly higher periostin levels as compared with females. Nevertheless, this discrepancy was not associated with the disease. The disease severity as measured by the SCORAD index was found to be weakly associated with disease duration and total Ig E levels only in the paediatric patient group. To summarize, these results implied that periostin levels might be associated with AD particularly in paediatric patients but that this association still needs to be evaluated in diverse populations also including different study parameters.

In the literature, there is only limited number of studies that evaluated the association of periostin levels with disease severity in patients with AD. One of these studies is the study by Sung et al., [19] in which the relation of serum periostin level with the severity

and chronicity of AD in children was evaluated. In their study, Sung et al., [19] reported that serum periostin level was significantly increased in children with AD and also found serum periostin level to be correlated with the severity and chronicity of AD in paediatric patients. The results of the present study were in partial accordance with the results reported by Sung et al., [19] as the periostin levels were not found to be associated with disease severity or disease duration in paediatric patients in the present study. Another study evaluating the relationship of plasma periostin levels with severity and chronicity of AD in paediatric patients was conducted by Ozceker et al., [20] The results of that particular study supported the association between periostin levels and AD but showed no association of periostin levels with severity or chronicity of AD in children and thus were in accordance with the results of the present study. In their study, Ghanem et al., [21] evaluated the significance of periostin levels in patients with AD and included paediatric patients aged between 3 and 18 years. They reported periostin levels to be significantly increased in patients as compared with controls, as was in the present study. On the other hand, unlike the results of the present study, they found periostin levels to be associated with disease severity and chronicity. In all of the above-mentioned studies, disease severity was measured using the SCORAD index, as was in the present study. As an overall interpretation, it can be suggested that periostin level may be a significant biomarker in patients with AD; however, population characteristics may influence the association of periostin with disease severity and chronicity in AD.

The number of studies on this issue for adult patients is scarce in the literature. To the best of our knowledge, Kou et al., [22] conducted the only study and evaluated the association of serum periostin level with clinical phenotype in adult patients with AD. They reported that periostin levels were significantly increased in the AD group and positively correlated with disease severity. They used Japanese guidelines for classifying the disease severity. Their results also revealed that periostin levels were correlated with eosinophil count but not with IgE levels [22]. In the present study, an association between periostin levels and AD could not be established in adults; the discrepancy between the result of our study and that of the study by Kou et al., [22] might be related to population characteristics.

Conclusion

AD is a multifactorial disease that is associated with multiple genetic and environmental interactions [23]. This multifaceted nature of the disease may also affect the biomolecular and clinical characteristics of the disease course. The results of the present study indicated the importance of periostin level in AD. Nevertheless, periostin level in AD still needs to be evaluated in further studies, which will include larger sample of patients with diverse backgrounds also including different study parameters.

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