www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i9.19

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Evaluation of Serum Level of Apelin in Patients with Atopic Dermatitis

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ABSTRACT

Background: *Atopic eczema (AE), also known as atopic dermatitis, is a chronic inflammatory skin disorder, characterized by cutaneous dryness, intense itching, scratching, skin damage, and secondary infections. Its cause remains unknown, although it is probably a combination of genetic, environmental, and immunologic factors. The prevalence of AE has risen substantially in many countries in recent decades, and this increase has been attributed mainly to changes in lifestyle, nutrition, and environmental factors.*

Aim of the work: *The aim of the work was toevaluate the serum level of Apelin in patients with atopic dermatitis and its correlation with disease severity in presence or absence of obesity.*

Subjects: The present study included twenty patients with atopic dermatitis, twenty patients with atopic dermatitis and obesity, twenty patients with obesity only and twenty age and sex matched normal control subjects. Venous blood samples were taken for measurement of serum concentration of apelin and IgE.

Results: *The results presented in our study demonstrate that a statistically significant difference in the level of apelin and statistically non-significant difference in level of IgE between four studied groups.*

Conclusion: *Our findings provided that apelin serum level increased with obesity and decreased with AD, with no correlation with both BMI and SCORAD which suggesting negative relation between apelin and severity of both diseases, also suggesting no association between severity of both diseases through our finding of no correlation between BMI and SCORAD.*

Keywords: *AD, apelin, IgE.*

INTRODUCTION

Atopic dermatitis (AD) or atopic eczema, is an inflammatory, chronically relapsing, and intensely pruritic skin disease occurring often in families with atopic diseases (atopic dermatitis, bronchial asthma and/or allergic rhino-conjunctivitis).(1) Less than 10% are regarded as severe cases because of disease intensity and extent (SCORAD > 40) or refractory

to treatment. Reasons for severe courses of AD are based on individual (e.g. genetic, barrier function, and allergies) risk factors and sometimes on therapeutic problems like misunderstandings with regard to topical treatment.[2] Management of exacerbated AD is a therapeutic challenge, as it requires efficient short-term control of acute symptoms, without compromising the overall management plan that is aimed at long-term stabilization, flare prevention, and avoidance of side effects.[3]

It is a complex disease that affects up to 20% of children and impacts the quality of patients and families in a significant manner. New insights into the pathophysiology of AD point to an important role of structural abnormalities in the epidermis combined with immune dysregulation.[4,5]

Apelin, a 36 amino acid peptide, is synthesized as part of a 77 amino acid prepropeptide precursor in specific hypothalamic neurons and appears to mediate its effects via a single G protein-coupled receptor subtype, the apelin receptor (APJ). In addition to apelin-36, other possible isoforms of the apelin peptide, including apelin-17, apelin-13 and the pyroglutamyl form of apelin-13 ([Pyr1]-apelin-13), also bind to and activate APJ (apelin receptor).[6]

Apelin and APJ mRNA are expressed in a variety of organs including brain, pituitary gland, heart, lung, adipose tissue and gastrointestinal tract, and are known key regulators of central and peripheral responses to multiple homeostatic perturbations.[7] These include regulation of fluid and cardiovascular homeostasis, the stress response, food intake, gastric cell proliferation and angiogenesis.[8]

Adipose tissue is far more than a site for energy storage and it is in fact an active endocrine, paracrine, and also immune organ secreting multiple bioactive mediators, called adipokines.[9] These adipokines include hormones (leptin, adiponectin), cytokines (TNF-α, IL-6, IL-10, and visfatin), and other proteins (apelin, resistin), which participate in numerous physiological and pathological processes. The deregulated synthesis and/or secretion of adipokines towards the proinflammatory compounds was observed in obesity and obesity-related disorders.[10]

Obesity has been shown to have several effects on the immune system, including preferential activation and trafficking of leukocyte subsets and pro inflammatory immune responses that might modulate the severity of atopic disorders, such as atopic dermatitis or asthma. Multiple studies demonstrated an association between obesity and asthma in children and adolescents, as well as wheeze. However, an association between obesity and atopic dermatitis has not been well established.[11-13]

MATERIALS AND METHODS

The aim of this study is to evaluate the serum level of Apelin in patients with atopic dermatitis and its correlation with disease severity in presence or absence of obesity.

The age of the patients included in this study ranged from 4-17 years with a mean equals 7.10 years in atopic patients, 9.10 years in atopic obese patients, 13.35 years in obese patients and 13.35 years in control, difference was statistically significant. Also in atopic patients, 6 males (30%) and 14 females (70%), in atopic obese patients, 5 males (25%) and 15 females (75%), in obese only patients, 2 males (10%) and 18 females (90%), while in control, 12 males (60%) and 8 females (40%) difference was statistically significant.

The present study included twenty patients with atopic dermatitis, twenty patients with atopic dermatitis and obesity, twenty patients with obesity only and twenty age and sex matched normal control subjects. Venous blood samples were taken for measurement of serum concentration of apelinand IgE.

Exclusion criteria included: The patients treated with any systemic (antihistamines, steroid) during the preceding 8 weeks or any topical (steroids, calcineurin inhibitors) for at least 1 week before enrolment into the study (emollients only allowed). Patients with concomitant asthma, rhinitis and

cardiovascular diseases was excluded from this study, to avoid any affection on Serum concentration of apelin and IgE.

All subjects were subjected to history taking with general and dermatological examination, serum level of apelin[14,15] and IgE[16,17] were measured using for both Enzyme-Linked immunosorbent assay (ELIZA).

RESULTS

There was a statistically significant difference in serum level of apelin in four studied groups with median level in atopic group 19.70, median level in atopic obese group 55.60, median level in obese group 177.90, while in control group was 150.75 with the highest level in the obese group which suggest the role of apelin in pathogenesis of obesity, but when we made a correlation between apelin and BMI it was irrelevant, which suggest the negative correlation between apelin and degree of obesity, while the lowest level was in atopic only group which suggest the increased level of apelin in the atopic obese group was related to obesity element not to the atopic one, and so after comparing with serum apelin level in control group we found that serum apelin level showed decreasing with AD when unopposed with elevating level caused by obesity, suggesting the role of apelin in pathogenesis of AD, while there was no correlation between apelin and SCORAD, which suggest that there was no role of apelin in the severity of AD. (Table 1, 2, 3, and Figure 1)

Table (1): Comparison between the four studied groups according to Apelin

	Atopic only (n= 20)	Atopic + obese (n= 20)	Obese Only (n= 20)	Control (n= 20)	$KW\chi^2$	p
Apelin (ng/ml)						
Min. – Max.	2.2 – 162.4	1.5 – 199.6	106.5 – 275.6	39.5 – 252.2		
Mean ± SD.	48.03±50.08	70.36±62.41	187.08±51.90	144.77±60.22	40.107*	<0.001*
Median	19.70	55.60	177.90	150.75		
$p_{control}$	<0.001*	0.001*	0.029*			
Sig. bet. grps.	p_1= 0.387 , p_2 <0.001* , p_3<0.001*					

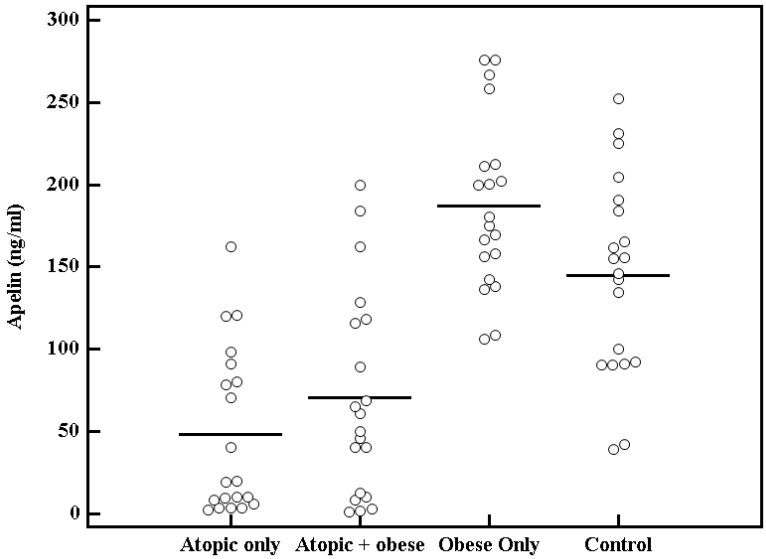

Figure (1): Comparison between the four studied groups according to Apelin

Table (2): Correlation between BMI and Apelin (ng/ml) in each group

	BMI	
	r	p
Apelin (ng/ml)		
Atopic only	0.116	0.627
Atopic + obese	-0.209	0.376
Obese Only	0.135	0.571
Control	0.094	0.692

Table (3): Correlation between SCORAD and Apelin (ng/ml) in each group

	SCORAD	
	R	p
Apelin (ng/ml)		
Atopic only	-0.308	0.186
Atopic + obese	-0.070	0.770

The difference in IgE serum levels in four studied groups was statistically non-significant with median IgE serum level in atopic only group 25.45, in atopic obese 59.70, in obese only 99.36, and in control was 151.15, and these may be correlated to the fact that the elevated concentrations of IgE are generally thought of in the context of allergic disease. (Table 4, Figure 2)

Table (4): Comparison between the four studied groups according to IgE

	Atopic only (n= 20)	Atopic + obese (n= 20)	Obese Only (n= 20)	Control (n= 20)	KW χ^2	p
IgE (u/ml)						
Min. – Max.	3.8 – 605.5	1.1 – 779.1	7.7 – 694.9	22.6 – 1195.1		
Mean ± SD.	128.58±198.07	152.55±206.02	152.13±186.72	263.15±336.47	7.481	0.058
Median	25.45	59.70	99.36	151.15		

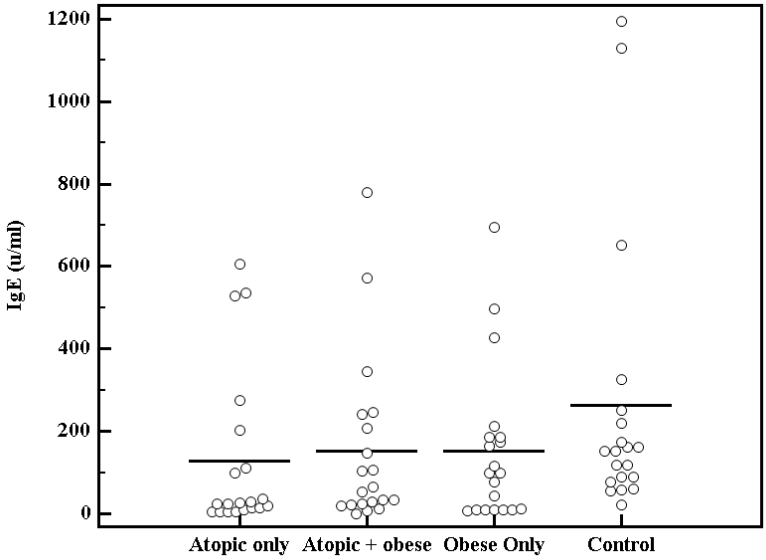

Figure (2): Comparison between the four studied groups according to IgE

No correlation was found between BMI and SCORAD that suggest there is no association between degree of obesity and severity of AD. (Table 5)

Table (5): Comparison between the two groups according to BMI and SCORAD

	Normal + Underweight (n = 20)	Overweight + Obese (n = 20)	t	p
BMI				
Min. – Max.	12.21 – 21.22	17.0 – 45.44		
Mean ± SD.	16.24 ± 2.29	23.14 ± 6.18	4.678*	<0.001*
Median	16.99	21.38		
SCORAD				
Min. – Max.	12.0 – 28.0	11.0 – 32.0		
Mean ± SD.	19.35 ± 4.86	19.60 ± 6.50	0.138	0.891
Median	20.50	19.0		

DISCUSSION

In this work there was a statistically significant difference in serum level of apelin in four studied groups with median level in atopic group 19.70, median level in atopic obese group 55.60, median level in obese group 177.90, while in control group was 150.75 with the highest level in the obese group which suggest the role of apelin in pathogenesis of obesity, but when we made a correlation between apelin and BMI it was irrelevant, which suggest the negative correlation between apelin and degree of obesity, while the lowest level was in atopic only group which suggest the increased level of apelin in the atopic obese group was related to obesity element not to the atopic one, and so after comparing with serum apelin level in control group we found that serum apelin level showed decreasing with AD when unopposed with elevating level caused by obesity, suggesting the role of apelin in pathogenesis of AD, while there was no correlation between apelin and SCORAD, which suggest that there was no role of apelin in the severity of AD.

EdytaMachura et al.[15] demonstrated in a previous single study of apelin in atopic dermatitis patients that serum levels of apelin were significantly higher in the total group of AD children than those of control group (P< 0.001), this study was carried out on 27children(mean age 9.9 ± 0.77 range 4.3–17.5y) with AD and the 46 healthy control subjects, Both groups were similar in age (P=NS). In AD group, 25.79% (n=6) of children were obese as well as 13.04% (n=6) in healthy children, also obese AD children had similar levels of apelin as normal-weight AD children, this study also proved that there was no correlation between apelin level and SCORAD.

In our study, the difference in IgE serum levels in four studied groups was statistically non-significant with median IgE serum level in atopic only group 25.45, in atopic obese 59.70, in obese only 99.36, and in control was 151.15, and these may be correlated to the fact that the elevated concentrations of IgE are generally thought of in the context of allergic disease. However, increases in the amount of circulating IgE can also be found in various other diseases, including primary immune deficiencies, infections, inflammatory diseases, and malignancies. Total IgE measurements have limited utility for diagnosis in only a subpopulation of patients with AD, the simple reduction in free IgE with associated anti-inflammatory effects is enough to achieve a clinical response. In only a subpopulation of patients with AD, the simple reduction in free IgE with associated anti-inflammatory effects is enough to achieve a clinical response. Stic evaluation of patients with suspected allergic disease, except for allergic broncho-pulmonaryaspergillosis (ABPA).[16]

Hotze et al.[17] studied the efficacy of omalizumab in moderate–severe AD, a target population of 20 adults (age range 23–76 years, nine men) to find that only a subpopulation of patients with AD, the simple reduction in free IgE with associated anti-inflammatory effects is enough to achieve a clinical response. Particular subgroup of patients with AD can benefit from anti-IgE treatment.

In our study we also found no correlation between BMI and SCORAD that suggest there is no association between degree of obesity and severity of AD.

Jeong et al.[18] demonstrated in a study carried out on rat model of AD by the Korea University College of Medicine Animal Research Policies Committee (KUIACUC-2009-134), that the decrease in immunological tolerance, evidenced by the increase in serum leptin and the decrease in adiponectin induced by juvenile obesity may be related to the aggravation of atopic dermatitis.

SUMMERY AND CONCOLUSION

In conclusion, the result of the present study could conclude that serum level of apelin was significant higher in obese non atopic group while lower in atopic non obese group, which may suggest the role of apelin in the etiopathogenesis of both AD and obesity. Additional prospective studies with a larger number of patients and application of other adipokines are needed to clarify the precise mechanism and their significance in the immune pathogenesis of AD.

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