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Research Article

Effect of Altitude on Serum Levels of Interferon Stimulated Gene-15 in Atopic Dermatitis Patients

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Abstract

Introduction: Atopic dermatitis (AD) is a chronic recurring, itchy, immuno-inflammatory skin condition. AD exacerbation can be motivated by seasonal and environment changes. ISG-15 plays an essential role in human immune system and can be used a marker for AD progression.

Materials and Methods: samples were collected from 107 AD patients including 53 living in high altitude city and 54 living at sea level. The levels of serum ISG-15 were detected using ELISA.

Results: serum level of ISG-15 was elevated in AD patients living in high altitude city comparing to the serum ISG-15 of AD patients living at sea level city. In addition, serum level ISG-15 was elevated in AD male patients living in high altitude city comparing to the serum ISG-15 of AD male patients living at sea level city.

Discussion and Conclusion: The finding is consistence with other research showing the effect of climate change on the progression of AD. Further investigation is required to understand the role of ISG-15 in this disease.

Keywords: Atopic Dermatitis; Interferon Stimulated Gene 15 (ISG-15); Eczema; High Altitude

Abbreviations

AD: Atopic Dermatitis; ISG-15: Interferon Stimulated Gene 15.

Introduction

Atopic dermatitis (AD) is a chronic recurring, itchy immuno-inflammatory skin condition, which affects both adults and children. AD has age-dependent clinical features, characteristic patterns and morphology of lesions [1]. Combination of factors cause aetiopathogenesis of AD that can predispose individuals to abnormal immune responses and dysfunctions in skin barrier when antigens contact the skin [2]. In addition, genetic factors play an important role patient's predisposition such as single nucleotide polymorphisms in some genes and mutations in the filaggrin gene reviewed in [3].

AD is highly heterogeneous inflammatory disorder of skin. The complexity of the disease portrayed by the advancement of genotyping and blood phenotyping which improve the understanding of the molecular mechanism of AD. For instant, 70% of AD patients have elevated IgE where most of them has eosinophilia [4]. In addition, the pathology of AD is assisted by the released cytokines and chemokines from activated keratinocytes [5]. This activation has a direct effect on type 1 interferon expression. Type I IFN increases rabidly the expression of ISG-15 [6-9]. ISG-15 gene is located in chromosome 1 cytoband 36.33 in human genome and the regulation of the gene I highly increased by interferon alfa and beta [10]. The protein of 17kDa plays an essential role in the immune system and elevated in tumours and viral infections [6-9]. It is useful marker as it can be detected in urine and in serum [11,12]. In

addition, the usefulness of serum ISG-15 as a marker for AD progression as ISG-15 was elevated in AD patients more than healthy control [13]. Serum ISG-15 were detected to have different effect among patients in Taif city [7,13-15].

Environmental factors include climate and weather conditions, volatile organic compounds, air pollutions and suspended bacteria and mold [16] The AD exacerbation can be motivated by seasonal and environmental changes surrounding the patients, such as occurs after a residential relocation or while on vacation [17]. In addition, climatic conditions play a potential role of in the aetiology of AD. Several studies of prevalence of AD in children in Australia, Japan and the United States showed that the prevalence was lower with higher humidity, warmer temperatures and increased sun exposure [2,17-19]. On the other hand, higher prevalence of AD was correlated with number of sunny hour, humidity and lower temperature in Spain [12]. Generally, the association of these studies with conflicting findings might be due to the regions where the studies were carried out. All of these regions are characterized by extreme change in weather during the four seasons of a year. In addition, it was recognized that the prevalence of AD is higher in developed countries comparing to developing countries. It was observed that the incidence of AD in developing countries is increased which might be due to the worldwide climate change. This change may trigger some subclinical diseases in predisposed individuals. In addition, it may exacerbate eczematous symptoms, which results in persistence or increased incidence of AD flares [19]. Lower humidity and warmer temperatures may promote epidermal dehydration and subsequently increase skin dryness, and hence further skin barrier dysfunction. These factors are altitude dependent where in higher altitude colder and drier air is observed. For instant, these features are noticed in Taif city which is a high-altitude city located in the western region of Saudi Arabia. It will be useful to find the relationship of the effect of living in such a city on the prevalence of AD and compare it with patients living in city located at sea level like Jeddah. The aim of this study is to investigate the effect of altitude on the level of ISG-15 in AD patients by comparing the serum level of ISG-15 in AD patients living in high altitude city and in see level city.

Materials and Methods

Study group

AD patients from two cities were participated in this study with written informed consent. The participants were from Taif (high altitude city) 27 male and 26 female, while 26 male and 28 female from Jeddah (sea level city). The age range for both groups were between 18 to 46 years. All subjects were free from any malignancy and viral infection. Also, all were using cortisone medications with different types and concentrations. The ethical approval was obtained from Taif University Ethical committee. Serum samples was collected from all participants and ISG-15 was analyzed.

ISG-15 serum levels

The collected serum was used to detect the level of ISG-15 using Human Interferon stimulated gene 15 ELISA Kit. The kit was used according to the manufacturer recommendation with detection sensitivity of 10 – 3000 ng (BT-laboratory cat no. E1988Hu). This analysis was performed using Bio-Rad xMark™ micro plate spectrophotometer.

Statistical analysis

The comparison of ISG-15 serum levels was performed using t-test. levels of the protein expression were compared between atopic dermatitis patients living at two different levels of altitudes and according to their gender. The comparison analysis and the graphs were produced using Paired t-test via GraphPad prism 5.03.

Results

Demographic analysis

This study included 107 AD patients participated from sea level city (Jeddah) and from high altitude city (Taif) including 54 and 53 patients respectively. The demonstration of the patient's demographic data is presented in Table 1.

	Taif		Jeddah	
	Male	**Female**	**Male**	**Female**
Number of patients	27	26	26	28
Minimum	19.0	18.0	19.0	18.0
25% Percentile	21.0	21.8	23.0	24.3
Median	24.0	26.5	28.0	30.0
75% Percentile	33.0	33.3	37.0	35.0
Maximum	46.0	45.0	46.0	46.0
Mean	27.8	28.5	30.6	30.1
Std. Deviation	8.8	8.2	8.0	7.6
Std. Error	1.7	1.6	1.6	1.4
Lower 95% CI	24.3	25.2	27.3	27.2
Upper 95% CI	31.3	31.8	33.8	33.1

Table 1: Demographic data analysis of the participants in this study.

Serum ISG-15 levels

The levels of ISG-15 in serum of AD patients were measured and compared according to the city of the patients' residency in this study. The mean level serum ISG-15 of AD patient living in Taif city (296.7 ng/ml) was significantly higher than the mean level ISG-15 of AD patients living in Jeddah city (237.5 ng/ml) (P value < 0.0018), Figure 1. In table 2 the statistical analysis of participants is illustrated.

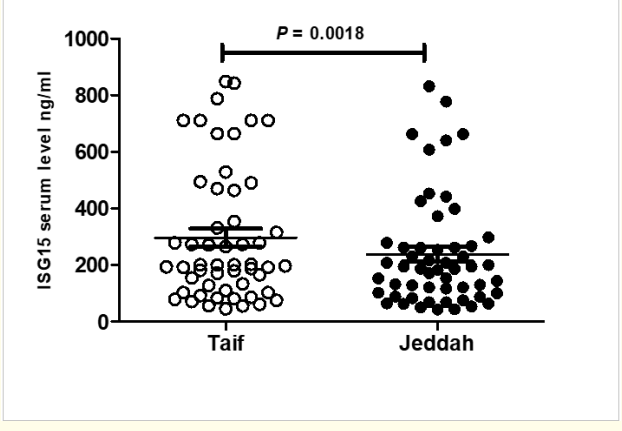

Figure 1: Serum ISG-15 levels comparison between AD patients living in Taif and AD patients living in Jeddah (P value =0.0018).

	Taif	Jeddah
Number of Patients	53	54
Minimum	45.0	43.0
25% Percentile	106.5	97.3
Median	200.0	186.5
75% Percentile	467.0	269.9
Maximum	849.0	832.0
Mean	296.7	237.5
Std. Deviation	236.0	195.5
Std. Error	32.4	26.6

Table 2: Statistical analysis of serum ISG-15 levels in the AD patients

Serum ISG-15 between genders

Comparison of serum ISG-15 level was performed according to the patient's gender and residency. Interestingly, the serum level of ISG-15 was higher in AD male patients living in Taif city comparing to AD male patients living in Jeddah city (P value = 0.0021), Table 3. on the other hand, there was no significant difference in the levels of serum ISG-15 in AD female patients living in both cities, Figure 2.

	Male-Taif	Male-Jeddah
Number of patients	27	26
Minimum	55.0	44.0
25% Percentile	110.0	110.0
Median	203.0	204.0
75% Percentile	354.0	323.3
Maximum	843.0	832.0
Mean	280.2	253.0
Std. Deviation	212.8	199.1
Std. Error	41.0	39.0
Lower 95% CI	196.0	172.6
Upper 95% CI	364.4	333.4

Table 3: Statistical analysis of serum ISG-15 levels in the AD male patients.

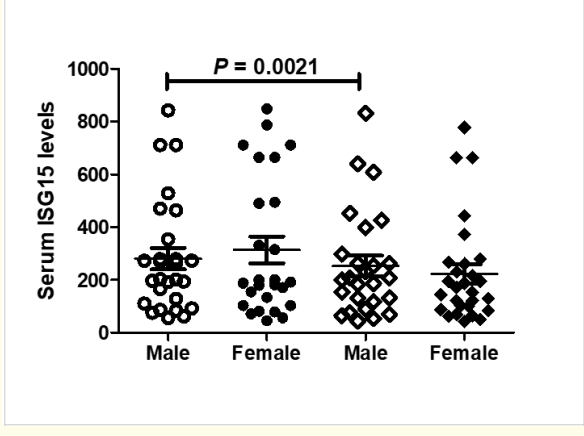

Figure 2: Comparison of serum ISG-15 level according to the patients' gender and location (Taif is on the left side).

Discussion

The aim of this study was to investigate the effect of altitude on the level of ISG-15 in AD patients. This was investigated by comparing the serum level of ISG-15 in AD patients living in high altitude city and in see level city. As the AD exacerbation can be motivated by seasonal and environmental changes surrounding the patients,

such as residential relocation or while on vacation [17]. Recently, AD incidence has increased rapidly, the prevalence of AD reach 20% in developed countries such as America and Australia [20]. Many factors contribute to the increased AD prevalence including environmental factors and genetical predisposition.

In high altitude areas, lower humidity, lower oxygen pressure, ambient air pollution and different temperatures are factors that may promote epidermal water loss and subsequently increase skin dryness, and hence further skin barrier dysfunction. These factors are altitude dependent where in higher altitude colder and drier air is observed. It was indicated that the prevalence was lower with higher humidity, warmer temperatures and increased sun exposure [2,17-19]. This is consistent with our findings in this study as the serum level of ISG-15 of AD patients living in Taif city (about 1800m above sea level) was significantly higher than the level ISG-15 of AD patients living in Jeddah city (about 30m above sea level). However, according to Suárez-Varela, higher prevalence of AD was correlated with number of sunny hour, humidity and lower temperature in Spain [12]. This conflict might be due to the seasonal time of the study as AD is disorder that highly triggered by environmental factors where it will be useful to monitor the progression of AD during seasonal changes [2,17-19].

ISG-15 is a marker for AD progression, our recent study has found significantly higher levels of serum-ISG1-15 in AD when it was compared to healthy controls. In addition, healthy AD male patients showed significantly higher levels than male controls [13]. Interestingly, in this study a consistent finding has been noticed where serum level of ISG-15 was higher in AD male patients living in Taif city comparing to AD male patients living in Jeddah city. This might be due to the increased skin exposure of male in Saudi Arabia to direct sun light and open areas where humidity is different comparing to closed area. However, further investigation is required to find out the role of ISG-15 in AD patients which can be as inducer for the pathogenesis of AD or protector and the source of this protein which might be the damaged cells of the skin.

Conclusion

Overall, this study has confirmed that the level of serum ISG-15 is elevated AD patients who are living in high altitude areas comparing to the level ISG-15 of AD patient living at lower altitude areas. This suggest the effectiveness of ISG-15 use as a biomarker for the progression of AD. However, further investigation is required to understand the exact role of ISG-15 in AD patient.

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Conflict of Interest

There are no financial interest or conflict of interest exists.

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Volume 3 Issue 6 June 2019