Original Article

Role of Periostin in Iraqi Asthmatic Patients

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Abstract

Background: Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. The understanding of the pathogenesis of the disease is essential to improve the plan of management. **Objective:** The objective of this study is to identify the role of periostin as inflammatory biomarker of asthma. **Materials and Methods:** A total of 200 participants were enrolled in the study, of which there are 100 controls and 100 asthmatic patients. Blood samples were obtained from the participants for periostin investigations by enzyme-linked immunosorbent assay assay. **Results:** Serum periostin concentrations were significantly ($P < 0.001$) higher in asthmatic patients (mean ± standard deviation [SD]; 68.152±9.792) compared to control group (mean ± SD; 46.488 ± 4.237). Periostin correlated negatively with forced expiratory volume (FEV) 1% and FEV1/forced vital capacity (FVC) in asthmatic patients. **Conclusions:** Serum periostin is increased in Iraqi asthmatic patients compared to controls and periostin correlated negatively with FEV1% and FEV1/FVC in asthmatic patients. Asthma is the most significant variable relates to high periostin serum concentration.

Keywords: Asthma, forced expiratory volume 1%, forced expiratory volume 1/forced vital capacity, periostin

Introduction

Asthma is a chronic inflammatory disease characterized by airway obstruction with hyperresponsiveness to variable stimuli, which is reversible by drugs or by itself.[1] Asthma attacks last from several minutes to several hours. Continuous asthma is the result of persistent obstruction of airways that will continue for days or weeks.[2]

Asthma is a major public health issue globally, affecting people of all ages, genders, and ethnicities. Globally, asthma is one of the most common chronic diseases worldwide, and it may affect as high as 334 million according to a report from the Global Asthma Network published in 2014.[3]

One common endotype of asthma is characterized by a type 2 inflammatory process that is perpetuated by the activity of type 2 cytokines. These include interleukin (IL)-4, IL-5, and IL-13, each of which can contribute to the pathogenesis of asthma.[4]

IL-13 directly contributes to many of the hallmarks of asthma pathophysiology, including mucus production, immunoglobulin E (IgE) class switching, subepithelial fibrosis, and airway hyperresponsiveness. IL-4 primarily promotes T-helper 2 cell differentiation and IgE class switching, whereas IL-5 promotes eosinophilia by promoting eosinophilopoiesis, eosinophil maturation, and survival.[5,6]

The wall of the airway in asthma is thickened by edema, cellular infiltration, and increased smooth-muscle mass and glands. With increasing severity and chronicity of the disease, remodeling of the airway occurs.[7] These changes are the result of epithelial cell alterations, subepithelial fibrosis submucosal gland hyperplasia, increased airway smooth muscle mass, and increased airway vascularization.[8]

Periostin synthesis by Bronchial and alveolar epithelial cell synthesis periostin is secreted by activated airway epithelial cells where it can access the vascular plexus in the subepithelial space and enter the peripheral bloodstream.[9]

Periostin is a protein that contains 836 amino acids with a molecular weight of 93.3 kD. Also named osteoblast-specific

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Submission: 26-05-2019 **Accepted:** 20-06-2019 **Published Online:** 25-09-2019

Access this article online

Quick Response Code:

Website: www.medjbabylon.org

DOI: 10.4103/MJBL.MJBL_39_19

How to cite this article: Al-Aaraji AJ, Al-Qaysi SA, Baay AS. Role of periostin in Iraqi asthmatic patients. Med J Babylon 2019;16:256-60.

factor 2, it was first described in 1993 and was named based on its expression in the periodontal ligament and periosteum of adult mice, and therefore renamed it periostin.[10]

The precise role of periostin in airway function is still unclear; however, periostin appears to contribute to several pathogenic processes in asthma, including subepithelial fibrosis, eosinophil recruitment, and mucus production from goblet cells. Subepithelial accumulation of periostin also promotes adhesion and motility of type 2–conditioned eosinophils and may serve as a guide for eosinophil migration in the extracellular matrix (ECM) in asthmatic airways.[11]

The potential role of periostin was given in eosinophil accumulation,[12] and it has been studied as a systemic biomarker for eosinophilic airway inflammation in asthma.[13] Using a logistic regression model, including fractional exhaled nitric oxide (FeNO), serum IgE, and blood eosinophils (other putative biomarkers of type 2 airway inflammation), high periostin was the best single predictor of airway eosinophilia in patients with severe asthma that was uncontrolled despite maximal inhaled corticosteroid (ICS) treatment.[14]

This work is, therefore, designed to investigate the influence of serum periostin concentrations in Iraqi asthmatic patients and also surveyed the correlation between serum periostin concentration and forced expiratory volume (FEV) 1% and FEV1/forced vital capacity (FVC) in asthmatic patients.

Materials and Methods

Subjects

The present study includes 200 patients. These patients were divided into two groups, the first group includes 100 asthmatic patients and the second group includes 100 apparently healthy individuals (control group).

The current study was carried out from the outpatients clinic (respiratory unit in Merjan teaching hospital/Hilla province, Iraq), and the samples were under the supervision of pulmonologist.

This study was performed in the laboratories of the Biochemistry Department in Faculty of the Medicine/ University of Babylon. In total, 100 asthmatic patients (65.64% of females and 34.35% of males) were enrolled in the study with FEV1/FVC <70 and FEV1% <80% of the predicted based on the Global Initiatives of Asthma Scale for Asthma Severity. Body Mass Index (BMI) was calculated by weight kg) divided by the square of height (m).[15] BMI = Weight (kg)/ Square Height (m^2).

Exclusion criteria were the presence of specific respiratory diseases such as cystic fibrosis and tuberculosis, identified by a physician, and the presence of other seriously interfering diseases. Were the presence age of Subjects <6 years, non agreement, smoker >10 pack years and the specific respiratory diseases such as cystic fibrosis and tuberculosis, identified by a physician, and the presence of other seriously interfering diseases. Patient with interstitial lung disease like Idiopathic pulmonary fibrosis, Drug-induced pulmonary fibrosis, chronic obstructive pulmonary disease, lung malignancy, bronchiectasis, in regard the periostin, the study exclude Bone fracture, Bone marrow fibrosis, any patient with documented hypertension, proved ischemic heart disease, proved heart failure, documented dyslipidemia patient and documented cancer patient or on chemotherapy.

Sample collection

Two milliliters of venous blood was taken from patients and drained into gel plain tube for serum preparation, which would be used in periostin test. Blood in gel tube was allowed to clot for 40 min at 37°C and then centrifuged at 3000xg for approximately 10 min.

The serum has been stored at −20°C till the time of assay. The concentrations of serum periostin were determined at laboratories of Biochemistry Department, Faculty of Medicine, University of Babylon by enzyme-linked immunosorbent assay (ELISA) using human periostin ELISA kit (PARS BIOCHEM).[16] The FEV1% and FEV1/FVC of all patients were recorded using spirometry.

Data analysis

The data were analyzed using the Software Package for Social Sciences version 21 (SPSS, IBM Company, Chicago, USA). The data were presented as a mean ± standard deviation (SD), the differences between studied groups were evaluated using unpaired Student's *t*-test. The associations between periostin level and FEV1% and FEV1/FVC were tested using Pearson's correlation coefficient.

Results

There was no significant difference in age and body mass index (BMI) (as mean) between control and asthma group (P = 0.652 and 0.786), mean ± SD for patients (36.34 ± 16.92 and 28.45 ± 7.22) and for controls (37.27 ± 10.27 and 28.20 ± 5.59) as shown in Table 1. This age and BMI matching helps to eliminate differences in parameter results that may originate due to the significant variation in age and BMI. Serum periostin concentrations were significantly (P < 0.001) higher in asthmatic patients (mean ± SD; 68,152 ± 9.792) than that of control group (mean ± SD; 46.488 ± 4.237) as illustrated in Table 2.

Table 1: Anthropometric parameters in studied groups (mean±standard deviation)

Variable	Study group	Mean±SD	*P*
Age (years)	Asthma	36.34±16.92	0.652
	Control	37.27±10.27	
BMI (kg/m^2)	Asthma	28.45±7.22	0.786
	Control	28.20±5.59	

SD: Standard deviation, BMI: Body mass index

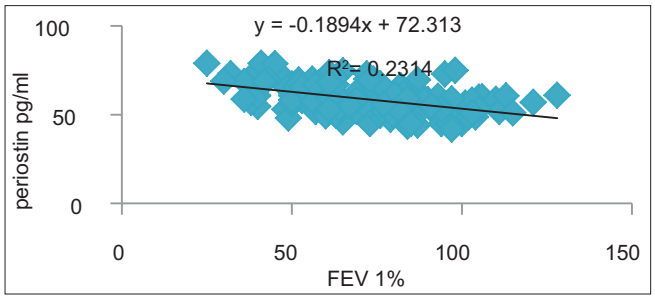

Figure 1: Correlation between periostin and FEV1% in patients' group

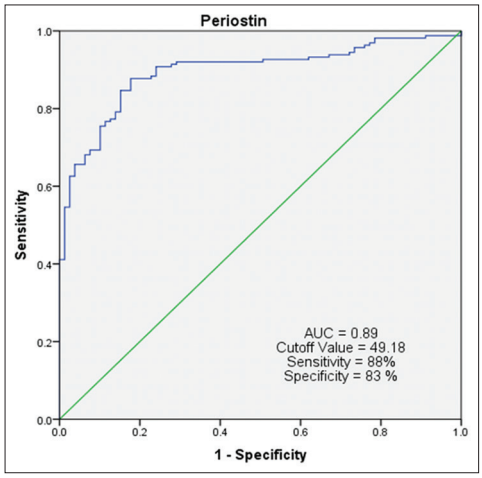

Figure 3: Receiver operating curve of serum level of periostin of patients group against control group. AUC: Area under the curve

Table 2: Mean difference periostin between asthmatic patients and controls

	Mean±SD		*P*
	Patients	Control	
Periostin pg/ml	68,152±9.792	46.488±4.237	<0.001

SD: Standard deviation

Periostin correlated negatively with FEV1% and FEV1/FVC. Figures 1 and 2 show a statistical comparison of periostin in studied groups.

Receiver operating curve analysis

Using receiver operating curve analysis, the periostin showed a good sensitivity and specificity in discriminating asthma from normal state with an area under the curve (AUC) of 0.89 with sensitivity of (88%) and specificity of (83%), as shown in Figure 3.

FEV1% showed a good sensitivity and specificity in discriminating asthma from normal state with an AUC of 0.81 with sensitivity of (82%) and specificity of (74%), At cut of value 49.18 pg/ml as shown in Figures 3 and 4.

Discussion

Asthma is a highly prevalent chronic respiratory disease.[16] The disease is characterized by airway inflammation, bronchial

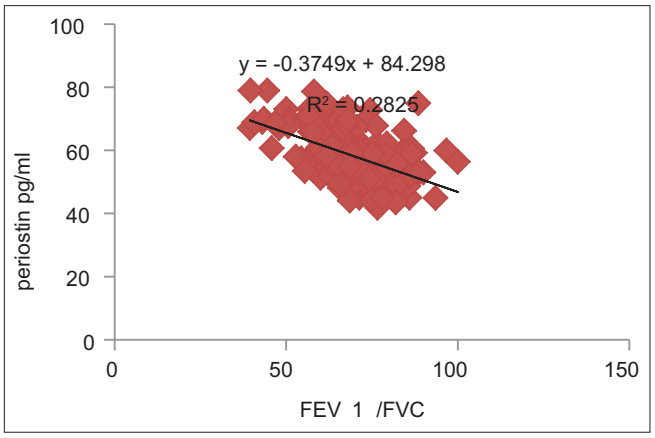

Figure 2: Correlation between periostin and FEV1/FVC in patients' group

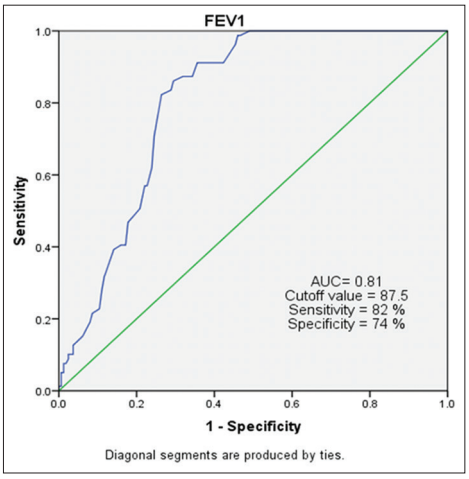

Figure 4: Receiver operating curve of FEV1% of asthmatic patients' group against control group. AUC: Area under the curve

hyperresponsiveness, and recurrent episodes of reversible airway obstruction.[16] The human airway bronchial epithelial cells, especially goblet cells, could be a source of serum and airway periostin, Table 2 shows a significant mean difference of periostin in asthmatic patients and control group with $P < 0.001$. This result was compatible with that of Jia *et al*. who reported that serum periostin levels were significantly higher in asthmatic patients.[14]

Moreover, the present findings are compatible with Bentley *et al*. who observed that in murine models, periostin has been linked to more severe asthmatic airway inflammation responses and hyperresponsiveness.[4] One cause of elevated serum periostin concentrations is correlated with a specific phenotype (eosinophilic asthma and late-onset asthma) and often complicated by obstructive pulmonary dysfunction.[17]

Periostin is involved in many aspects of asthma as well, including eosinophil recruitment,[18] airway remodeling, and development of a Th2 phenotype and contributes to the increased expression of inflammatory mediators.[19]

Furthermore, the concentrations of FEV1% and FEV1/FVC were a significant statistical decrease in asthmatic patients

compared to the control group. These data are supported by the report of Bremner *et al*. that increased bronchial responsiveness associated with lower levels of lung function.[20]

In addition, Kanemitsu *et al*. published their findings and discovered that the serum periostin concentrations coordinate with an annual downturn in FEV1%, independent of the severity of asthma.[21] Previously, Blanchard *et al*. showed that periostin accelerates allergen-induced eosinophil recruitment in the lung and esophagus,[12] whereas Sehra *et al*. and Gordon *et al*. demonstrated that periostin protects mice from allergic airway inflammation.[22,23]

In one preliminary study, in which 20 patients with asthma were followed up for 20 years, the amount of periostin deposition and the numbers of cells positive for osteopontin (another ECM protein) in the bronchial subepithelium were associated with a long-term decline in FEV1%.[24]

In a multi-center cohort study of 224 patients with asthma receiving ICS, polymorphisms in the POSTN gene were related to higher serum periostin levels and a decline in FEV1% of >30 ml/year.[21]

Among several serum biomarkers, including high-sensitivity C-reactive protein and eosinophil cationic protein, periostin was the only marker associated with an accelerated decline in FEV1% (>30 ml/year): high serum periostin levels were significantly correlated with a greater annual decline in FEV1%.[21]

Furthermore, the association between serum periostin and a decline in FEV1, despite ICS therapy, was found to be most evident in the cluster characterized by patients with late-onset asthma and severe eosinophilic inflammation.[25]

Taken together, these findings suggest that serum periostin has the potential to be clinically validated for used as a prognostic biomarker to predict the risk of lung function decline, particularly in patients with late-onset and eosinophil-dominant asthma. The results of a substudy of the aforementioned cohort trial suggested that high serum periostin could also be used as an additional biomarker to improve the identification of ICS-insensitive patients among those with elevated FeNO, whereas ICS-insensitive patients are defined as those with an accelerated decline in FEV1% or a risk of asthma exacerbations despite receiving high-dose ICS treatment.[26]

One of previous study observed that patients with high serum periostin concentrations had low FEV1% and FEV1/FVC in spite of shorter duration of asthma confirms that periostin is a biomarker of rapid decline in pulmonary function,[27,28] and this observation agreement with the present study.

Conclusions

Serum periostin is increased in Iraqi asthmatic patients compared to control group and periostin correlated negatively with FEV1% and FEV1/FVC in asthmatic patients. Periostin may be considered as a biomarker to distinguish asthmatics from nonasthmatics individuals.

Ethical clearance

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. The study protocol and the subject information and consent form were reviewed and approved by a local Ethics Committee.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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