



# Clinical Utility of Serum Periostin as Biomarker of Differential Diagnosis for Different Phenotypes of Bronchial Asthma

Haji Muhammad Rashid<sup>1\*</sup>, Mudassar Khan<sup>2</sup>, Jamal Khan<sup>2</sup>, Muhammad Aamer Suggad<sup>3</sup>, Hiza Hassan<sup>2</sup>, Hasanat Khan<sup>2</sup>, and Mehreen Akhlaq Abbasi<sup>4</sup>

<sup>1</sup>Department of Chemical Pathology, University of Health Sciences, Lahore, Pakistan

<sup>2</sup>Department of Medical Lab Technology, University of Haripur, Haripur, Pakistan

<sup>3</sup>Department of Pathology, The Children Hospital & The Institute of Child Health, Multan, Pakistan

<sup>4</sup>Institute of Allied Health Sciences, University of Azad Jammu & Kashmir, Muzaffarabad, Azad Kashmir

**Abstract:** Periostin is a protein produced from epithelial cells of the respiratory tract in response to the stimulation from IL-13. Periostin levels in serum are associated with its production in airways. This study was conducted to evaluate the clinical utility of serum periostin levels in the differential diagnosis of atopic and non-atopic asthma. This cross-sectional comparative study was carried out at Medsol Clinical Laboratory, Islamabad on 40 healthy individuals as control (Group A) and 40 asthmatic patients (Group B) from Jan-2020 to Aug-2020. Group B was comprised of 20 atopic asthmatic patients (Group BI) with positive skin prick test and 20 non-atopic asthmatic patients (Group BII) with negative skin prick test. Demographic data were obtained on proforma, lung function test and skin prick test was performed at pulmonologist clinic. EDTA and clotted blood samples were obtained from all participants to measure absolute eosinophil count (AEC) and periostin levels. Serum periostin levels were significantly higher in asthmatic patient Group B ( $396 \pm 84$ ) than healthy controls Group A ( $185 \pm 40$ ). In asthmatic groups, serum periostin levels were significantly higher in group BI (atopic asthmatic) than group B II (non-atopic asthma). There was a strong association between serum periostin and AEC (0.83), serum periostin, and FEV1 (-0.81) in atopic asthmatic patients. We concluded that serum periostin can be used for the diagnosis of bronchial asthma and a good purposed biomarker for differential diagnosis of different phenotypes of asthma.

**Keywords:** Asthma, Phenotypes, T2 disease, Non-T2 disease, Periostin, Atopy, Eosinophils, Th2 Inflammation.

## 1. INTRODUCTION

Asthma is a respiratory disease with chronic inflammation of the respiratory tract, which is associated with airways contraction, chest tightness, wheezing, cough, mucus production, abnormal lung function test and remodeling of airways which causes difficulty to breathe and limit the daily activity of the patient [1]. Asthma severity is described in terms of frequency of episodes in day and night time and duration of episodes of asthmatic exacerbation [2]. Asthma is one of the most prevalent disorders; about 4.3% population is suffering from asthma around the world [3]. The

prevalence of severe asthma is 0.1% among the general population [4]. Depending on the underlying mechanism of pathophysiology, asthma is classified into Atopic and Non-Atopic [5]. Atopic asthma is allergic asthma and mostly occurs in childhood and it is the most prevalent form associated with more than 75% of total asthmatics cases [6], while non-atopic asthma is non-allergic with unknown pathophysiology [7].

Periostin is a protein that is expressed in the extracellular matrix of fibroblasts or epithelial cells of the airway. Periostin expression is induced in fibroblasts by T-helper cell type 2 (Th2) cytokines,

which may cause sub-epithelial fibrosis in asthma [8]. It is reported that levels of serum periostin could be a biomarker of eosinophilic inflammation of the airways in severe asthma in adults [9]. Epithelial cells of airways, fibroblasts, and eosinophils express periostin under rest conditions [10]. However, the pattern of expression can be altered in the case of airway inflammation. The role of periostin in asthma is still unknown. Previous studies indicated that periostin works as a protective molecule against allergic inflammation [11]. But currently, it is reported that periostin accelerates allergic airway inflammation, using periostin-deficient mice and neutralizing antibodies against periostin [12]. Decreased lung function in asthma along with deposition of periostin in biopsy is inversely associated, which supports the idea that periostin is an accelerator for bronchial asthma [13]. This study aimed to evaluate the clinical utility of serum periostin levels in the differential diagnosis of atopic and non-atopic asthma and to measure FEV1, AEC, and serum periostin levels in asthmatic (both atopic and non-atopic) and non-asthmatic adults

## 2. METHODOLOGY

This cross-sectional comparative study was carried out at Medsol Clinical Laboratory, Islamabad on 40 healthy individuals as controls (Group A) and 40 asthmatic patients (Group B). Group B was comprised of 20 atopic asthmatic patients (Group BI) with positive skin prick test and 20 non-atopic asthmatic patients (Group BII) with negative skin prick test. Informed consent was taken from all participants. Demographic data were obtained on a proforma. Lung function tests and skin prick tests were performed at the pulmonologist clinic. Venous blood samples were collected in EDTA (for whole blood) and gel vials (for serum) from all participants to measure absolute eosinophil count (AEC) and periostin levels. Complete blood count (CBC) was performed on Mindray BC-5000 (automated hematology analyzer) to obtain AEC. Serum samples were stored at 20°C till the measurement of periostin levels. Serum periostin levels were measured by ELISA (Enzyme-Linked Immunosorbent Assay). A pulmonary function test was performed with a spirometer for forced expiratory volume (FEV1), which measures the expired volume in one second. Skin prick tests were performed according to standard methods

with allergens, histamine-positive and negative controls purchased from Creative Drug Industries [14]. Patients with >3mm circles of indications were considered positive for atopy and < 3mm were negative.

**Exclusion Criteria:** Patients with other concomitant chest diseases (chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis), chest infection, malignancy, and patients with cardiac diseases were excluded.

## 3. RESULTS

Asthma is more prevalent in females, 60% of asthmatic patients in our study were females. Smokers or ex-smokers are also at risk to develop asthma. Socioeconomic status is also associated with asthma. In our study, 50% of asthmatic patients were from lower socioeconomic status (Table 1).

Table 2 shows that eosinophil and periostin levels were higher and FEV1 was lower in the patient

**Table 1.** Demographic characteristics of participants

Variables	Group A (n = 40)	Group B(n = 40)
Gender		
Males	16(40%)	18(45%)
Females	24(60%)	22(55%)
Age(years)	46.4 ± 7.3(34-62)	46.5 ± 5.4 (34-56)
Smoking Status		
Non-Smokers	30(75%)	28(70%)
Smokers or Ex-Smokers	10(25%)	12(25%)
Socioeconomic Status		
Rich	8(20%)	6(15%)
Medium	12(30%)	14(35%)
Low	20(50%)	20(50%)
Forced expiratory Volume (FEV1 %)	68.0 ± 6.4	97.0 ± 1.9

group (Group B) than in the control (Group B). There were significant differences between the two groups.

Table 3 shows that eosinophil and periostin levels were higher and FEV1 was lower in atopic asthmatic patients (Group BI) than non-atopic asthmatic patients (Group BII). There was a significant difference between the two groups.

A significant correlation was found between serum periostin and AEC in both groups, but this association was stronger for Group BI ( $r^2= 0.83$ ) than Group BII (0.67) as shown in Fig 1.

A significant negative correlation was found between serum periostin and FEV1 in both groups, but this association was stronger in Group BI (-0.81) than Group BII (-0.63) as shown in Fig 2.

Table 2. Comparison of AEC, Serum Periostin, and FEV1 between asthmatic patients (Group A) and non-asthmatic individuals (Group B).

Variables	Group A	Group B	P-Value
AEC	174 ± 62	396 ± 84	<0.001
Periostin	185 ± 40	356 ± 103	<0.001
FEV1%	97.0 ± 1.9	68.0 ± 6.4	<0.001

Table 3. Comparison of AEC, serum periostin, and FEV1 between atopic asthmatic patients (Group B I) and non-atopic asthmatic patients (Group BII).

Variables	Group B i	Group B ii	P-Value
AEC	440 ± 95	334 ± 65	<0.001
Periostin	391 ± 140	306 ± 73	<0.001
FEV1%	72 ± 6.3	66 ± 7.4	<0.001

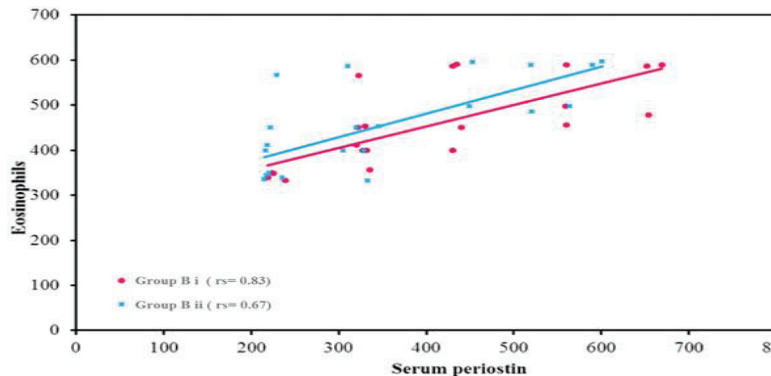


Fig.1. Correlation of serum periostin with AEC in atopic asthmatic patients (Group B i) and non-atopic asthmatic patients (Group B ii).

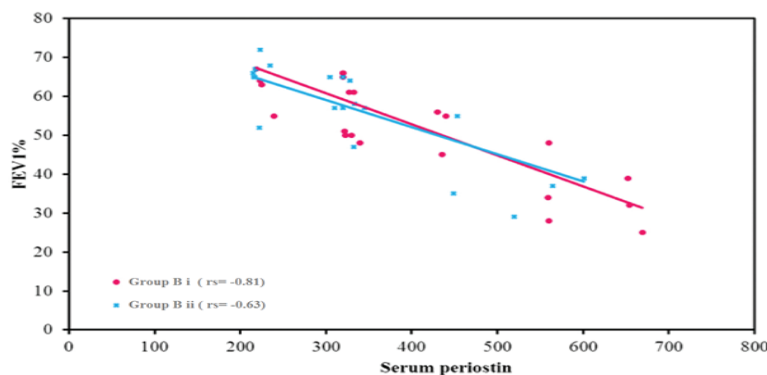


Fig. 2. Correlation of serum periostin with FEV1 in atopic asthmatic patients (Group B i) and non-atopic asthmatic patients (Group B ii).

#### 4. DISCUSSION

In the present study, it was found that asthma is more prevalent in females i.e. 60% of asthmatic patients. A gender disparity exists in asthma prevalence. As adults, women have an increased asthma prevalence compared to men. Further, women are more likely to have severe asthma and later onset of asthma compared to men [15]. Socioeconomic status also contributes to the prevalence of asthma, as in our study there were 50% of asthmatic participants were from low socioeconomic status. Peoples with low socioeconomic status may have higher exposure to indoor asthma factors (e.g., cockroaches, tobacco smoke) and outdoor asthma factors (e.g., urban pollution); that is why they have a higher tendency to develop asthma [16]

In our study, we found that eosinophil count was higher in the patient group than the control group, as there were significant differences between the two groups ( $P < 0.001$ ) shown in table 2. In agreement with these results, Inoue et al [17] reported that there were highly significant differences between patients and controls regarding blood eosinophil, as it was higher in the patient group (Group B).

Results of this study revealed that serum periostin levels were higher in group BI (atopic asthma patients) followed by group BII (non-atopic asthma patients), with lower levels in controls (Group A); this shows that there were statistically significant differences among the three groups regarding serum periostin ( $P < 0.001$ ). In agreement with our results, Inoue et al. [17] reported that the serum periostin levels were higher in the asthmatic group than in the control group [17, 18]. We observed a strong positive association between serum periostin and AEC, and a strong negative association between serum periostin and FEV1 in both asthmatic groups (atopic and non-atopic), but the associations of periostin levels were more strong in atopic asthmatic patients (Fig 1 and Fig 2). A similar association of serum periostin was reported in previous studies [17, 18] that there is a positive correlation between serum periostin and other biomarkers of type 2 immunity such as blood eosinophil count and FeNO in childhood and adult asthma. Atopic asthma is associated with Th2/T2 inflammation and eosinophilia [19], which induces the production of IL-3, that stimulate the release of periostin from endothelial and fibroblast cells of airways [20], while non-atopic asthma works on the un-known mechanism and Th2-T2

inflammation or eosinophilia is less common, that is why serum periostin levels are low in non-atopic asthma [21].

#### 5. CONCLUSION

We concluded that serum periostin increases in patients with asthma and is higher in atopic than non-atopic patients and can be considered as a diagnostic biomarker of bronchial asthma; and along with AEC, the serum periostin may be useful for differential diagnosis of atopic and non-atopic asthma. These findings are particularly useful for developing therapeutic approaches to different phenotypes of asthma.

#### 6. RECOMMENDATIONS

Large scale studies are required to establish serum cut off values for different phenotypes of asthma, and different severity levels of asthma.

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