Asthma phenotype: Clinical, physiological, and biochemical profiles of North Indian patients

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ABSTRACT

Background and Objectives: Asthma is a common, chronic and heterogeneous disease with various phenotypes. The clinical phenotypes have aided in revealing the genetic heterogeneity, provide education, lifestyle advice and novel biological treatments. The few common factors associated with phenotypes are smoking, rhinitis and obesity. The present study was thus planned to analyse and correlate the clinical, physiological, biochemical and serological parameters of asthma and to study the phenotypic characteristics in different asthmatic. Methods: This was a prospective observational study of 120 patients with 30 each in BA-rhinitis, BA, BA-obesity and BA smoker phenotypes. All the enrolled patients were assessed by SGRQ, Mini-AQLQ, GINA with ACE, chest X ray, Spirometry, SPT against common aero-allergens, FENO, hsCRP, vitamin-D, IgE, and Interleukins (IL) including IL-5, IL-6, IL-8, IL-13, IL-17 and IL-33. The mentioned profiles of each phenotype correlated and characterized among different phenotypes. Results: The majority of patients 78(65%) were female with mean BMI of 24.07±4.73kg/m². Majority of the patient in BA and BA-rhinitis phenotype are in mild severity and young compared to majority in BA-obesity and BA-smoker are moderate to severe with older. (p<0.001) The SPT and FENO level were highest among BA-rhinitis phenotype with significant difference among phenotypes. (p<0.001) Similarly the most of inflammatory markers were significantly different in various phenotypes. The FEV1 showed correlation with most of parameters with statistically significant correlation with IL-5, IL-8 and FENO. Conclusion: The majority of parameters were significantly different among various phenotypes. We advise to phenotypic classification of asthma whenever possible for better management and quality of life.

KEY WORDS: Asthma, obesity, phenotype, rhinitis and smoker

INTRODUCTION

Bronchial asthma (BA) is a common, chronic, and heterogeneous disease with different presentation, disease progression, and response to therapy carrying a significant mortality and high morbidity.[1] Asthma is a series of complex, overlapping individual disease, or phenotypes, each defined by its unique interaction between genetic, environments, and associated comorbid factors. Asthma management must be individualized, tailored not only to the severity of disease but also the phenotypic characteristics of the disease. A good understanding of phenotypic characteristics is enough to provide education and lifestyle advice and to base treatment on the phenotype as well as severity and control of disease. It is promising that identification of the clinical phenotypes of asthma has...
aided in revealing the genetic heterogeneity of the disease. The use of biological markers in the analyses would give us more detailed information on disease pathogenesis and open possibilities for novel treatments. Numerous environmental factors including infection, smoking, obesity, and others still to be identified can influence an underlying immune-inflammatory process in asthma.\textsuperscript{[2,3]}

The few common factors associated with asthma phenotypes are smoking, rhinitis, and obesity. Smoking increases oxidative stress and has pro-inflammatory effects on the lungs of nonasthmatics. These are changes predisposing for development of asthma. Smoking increases number of airway inflammatory cells (neutrophils and macrophages), as well as inflammatory cytokine.\textsuperscript{[4]} Allergic rhinitis is ubiquitous in patients with allergic asthma, and is an important characteristic of the allergic asthma phenotype. Recent investigations have demonstrated that allergic and nonallergic upper airway disease are both risk factors for developing asthma and are present in the majority of patients with asthma. Thus, both the presence and treatment of rhinitis may significantly affect the asthma phenotype.\textsuperscript{[5]} Obesity has also been found to be a risk factor for developing asthma in individuals with and without allergy. Furthermore, it is known that obesity may worsen preexisting asthma, through both biochemical and mechanical effects, and potentially impair response to treatment.\textsuperscript{[6]}

The present study was thus planned to analyze and correlate demographic, clinical, quality of life, lung function, and inflammatory markers in different groups of asthma and to study the phenotypic characteristics in different asthmatic groups which might help for the better management and targeted therapies.

**MATERIALS AND METHODS**

This was a prospective observational study of asthma patients diagnosed by the Global Initiative for Asthma (GINA) 2016 guidelines.\textsuperscript{[7]} The study was done after the approval of the Institutional Ethical Committee in the Department of Pulmonary Medicine at Vallabhbhai Patel Chest Institute, University of Delhi, from April 2017 to March 2018. The voluntary, informed consent was taken from all the patients. Pregnant and lactating females, less than 18 years, and cognitive impairment patients were excluded from this study. The enrolled patients were divided into the following four groups with thirty cases in each group: (1) BA with smoker (>10 pack-years),\textsuperscript{[4]} (2) BA with rhinitis,\textsuperscript{[5]} (3) BA with obesity (WHO Asian body mass index [BMI] criteria),\textsuperscript{[6] and (4) BA without rhinitis, obesity, and smoking. All the enrolled patients were assessed clinically, serologically, physiologically, and biochemically. The clinical assessment was done by using St. George’s Respiratory Questionnaire (SGRQ), Mini-Asthma Quality of Life Questionnaire (Mini-AQLQ), and GINA asthma severity.\textsuperscript{[7-9]} The physiological, biochemical, and serological assessment was done with complete blood counts with absolute eosinophil count (ACE), chest X-ray posterior-anterior view, spirometry with reversibility, skin prick test (SPT) against common aeroallergens, fractional exhaled nitric oxide (FeNO), and serology markers including highly sensitive C-reactive protein (hsCRP), Vitamin D, total immunoglobulin E level, and interleukins (ILs) including IL-5, IL-6, IL-8, IL-13, IL-17, and IL-33. The detail patients enrollment is shown in Figure 1.

**Spirometry**

Spirometry was conducted on a dry, roll-seal spirometer of the Benchmark design lung function machine (PK. Morgan, Kent, UK). Full expiratory flow-volume curves have been produced as suggested by ATS. Forced expiratory volume in 1 s (FEV\textsubscript{1})/forced vital capacity was taken for assessing the obstruction, and FEV\textsubscript{1} was taken for assessing the severity of asthma.\textsuperscript{[10]}

**Skin prick tests**

It was performed with a battery of 58 common aeroallergen allergens. The allergen extracts (1:10 w/v, 50% glycerinated) were procured from All Cure Pharma Pvt. Ltd., New Delhi. The skin test reactions were graded as per Indian standard protocol.\textsuperscript{[11]}

**Serology markers**

All the abovementioned serology markers in the patient’s serum were determined by enzyme-linked immunosorbent assay with standardized kits according to the manufacturer’s protocol.

We analyzed the above clinical, physiological, biochemical, and serological profiles in each phenotype of patients and correlated and characterized it among different phenotypes. We also did the correlation of FEV\textsubscript{1} with all serological markers.

**Statistics**

The continuous data are presented as numbers, percentage, mean, and standard deviation. Figures are presented as bar diagram and table. To test the difference among groups, post hoc multiple comparisons are applied. Chi-square test is also used for comparison among subgroups. The correlation coefficient was calculated by Pearson’s correlation method. \( P < 0.05 \) was considered statistically significant.

**RESULTS**

A total of 120 asthma patients with 30 each in 4 different phenotypes were enrolled. The overall majority of patients 78 (65%) were female and the remaining 42 (35%) were male. The predominance of female patients was seen in all phenotypes. The age group of patients was different among various phenotypes. Among the BA and BA-rhinitis phenotypes, the commonly affected age group was 20–30 years, while among the BA-smoker and BA-obesity,
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The overall mean BMI of all asthma patients was 24.07 ± 4.73 kg/m². The BMI was maximum in BA-obesity phenotype and minimum in BA phenotype with statistically significant difference between various phenotypes. Majority of the patients (70%–90%) in BA and BA-rhinitis phenotypes are in intermittent and mild persistent severity, while all the patients in BA-obesity phenotype are in persistent severity except one. All the BA-smoker phenotype patients are moderate-to-severe persistent severity. The difference in severity of asthma at presentation was found to be statistically significant among various phenotypes (P < 0.001). The severity of asthma is a milder form in BA-rhinitis phenotype and severe in BA-smoker phenotype. The details of severity are shown in Figure 2.

The mean value of SGRQ questionnaire was 28.08 ± 12.30 in BA-rhinitis, 34.28 ± 17.42 in BA, 49.38 ± 21.92 in BA-obesity, and 63.22 ± 9.32 in BA-smoker phenotype. The score was lowest in BA-rhinitis and highest in BA-smoker phenotype. The difference in SGRQ score between the groups was statistically significant (P < 0.001). The mean value for Mini-AQLQ was 4.93 ± 0.52 in BA-rhinitis, 5.24 ± 0.67 in BA, 3.64 ± 0.90 in BA-obesity, and 2.90 ± 0.51 BA-smoker phenotype. The score is lowest in BA-smoker and highest in BA-rhinitis. The difference in Mini-AQLQ score between the groups was of statistically significance (P < 0.001) [Figure 3 and Table 1].

The SPT positivity in BA-rhinitis, BA, BA-obesity, and BA-smoker was 27 (90%), 4 (13.33%), 14 (46.67%), and 5 (16.67%), respectively. The SPT positivity was maximum in BA-rhinitis phenotype and lowest in BA phenotype. The difference in positivity to SPT against aeroallergen in asthma patients was statistically significant among the different phenotypes (P < 0.001). The overall common aeroallergens positive were insects in 20 and house dust mite (HDM) in 19 patients. The detail of different antigen positivities in various asthma phenotypes is shown in Figure 4. The spirometry with reversibility was done in all 120 patients at presentation. The overall spirometry was normal in 26 (21.6%) and obstructive pattern in 96 (78.3%) patients. The obstructive abnormality was mild in 32 (34%), moderate in 41 (43.6%), and severe in 21 (22.4%) patients. The severity of obstruction was different among various phenotypes, as shown in Figure 5. All the patients enrolled with obstructive pattern on spirometry showed significant bronchodilator reversibility. The mean value of FEV1 for the BA-rhinitis, BA, BA-obesity, and BA-smoker phenotypes was 86.43 ± 11.85%, 78.62 ± 16.88%, 65.31 ± 17.45%, and 59.74 ± 14.03%, respectively. The P value derived for this variable between the groups is statistically significant (P < 0.001). The mean value of FeNO was 45.67 ± 19.07 ppb in BA-rhinitis, 28.90 ± 15.65 ppb in BA, 28.97 ± 20.37 ppb in BA-obesity, and 20.00 ± 8.68 ppb in BA-smoker phenotype. The FeNO level was statistically significant among different phenotypes (P < 0.001). It

Figure 1: The detail of patient enrollment

Figure 2: Distribution of asthma severity in different phenotypes. Majority of the BA and BA-rhinitis phenotype patients are in intermittent and mild persistent severity. While almost all BA-obesity and smoker phenotypes are in moderate-to-severe persistent severity.
was maximum in BA-rhinitis phenotype and lowest in BA-smoker phenotype [Table 1].

We also did the correlation of FEV1 with hsCRP, IL-5, IL-6, IL-8, IL-13, IL-17, IL-33, Vitamin D, AEC, and FeNO. The FEV1 showed a statistically significant positive correlation with IL-5 ($P = 0.002$, $r = 0.277$) and FeNO ($P = 0.050$, $r = 0.176$) while a significant negative correlation with IL-8 ($P = 0.050$, $r = -0.179$). While other markers showed no significant correlation with FEV1. The details of FEV1 and its correlation with other parameters are shown in Figure 6 and Table 2. The age, BMI, SGRQ, AQLQ, eosinophilic/lymphocyte (E/L), and eosinophil/neutrophilic (E/N), FEV1, FeNO, AEC, IL-5, IL-6, IL-8, IL-13, IL-17, and IL-33 parameters were measured and compared in different asthma phenotypes. Majority of inflammatory parameters including FeNO, ACE, IL-5, and IL-13 were highest in BA-rhinitis phenotype. The IL-6 and IL-33 were highest in BA-smoker phenotype, while IL-8 was highest in BA-obesity and IL-17 in BA phenotype patients Figure 7. All the parameters except IL-6, IL-13, IL-17, and IL-33 showed statistically significant $P$ value in different asthma phenotypes. The details of all parameters with different phenotypes are shown in Table 1. This cut part of paragraph should be at the start of paragraph on right side before the sentence “The age, BMI, SGRQ, AQLQ, eosinophilic/lymphocyte (E/L), and eosinophil/neutrophilic (E/N), FEV1, FeNO, AEC, IL-5, IL-6, IL-8, IL-13, IL-17, and IL-33 parameters were measured and compared in different asthma phenotypes”.  

**DISCUSSION**

In the present study, we found that the difference in severity of asthma at presentation was different

### Table 1: Details of various clinical, biochemical, and serological parameters in different asthma phenotypes

| Parameter, mean±SD | BA-rhinitis | BA | BA-obesity | BA-smoker | $P$ |
|---------------------|-------------|---|------------|-----------|-----|
| Age (years)         | 30.80±7.86  | 34.10±12.59 | 39.17±12   | 54.00±9.23 | <0.001 |
| BMI (kg/m²)         | 21.20±2.33  | 20.87±2.36 | 29.68±3.5  | 21.55±3.03 | <0.001 |
| SGRQ                | 28.08±12.3  | 34.28±17.42 | 49.38±21.92 | 63.22±9.32 | <0.001 |
| AQLQ                | 0.94±0.52   | 5.24±0.67  | 3.64±0.9   | 2.90±0.51  | <0.001 |
| E/L ratio           | 0.26±0.11   | 0.15±0.08  | 0.19±0.1   | 0.13±0.07  | <0.001 |
| E/N ratio           | 0.14±0.07   | 0.08±0.04  | 0.11±0.06  | 0.07±0.04  | <0.001 |
| FEV1 (%pred)        | 86.43±11.85 | 78.62±16.88 | 65.31±17.45 | 59.74±14.03 | <0.001 |
| FeNO (ppb)          | 45.67±19.07 | 28.90±15.65 | 28.97±20.37 | 20.00±8.68  | <0.001 |
| AEC (cells)         | 586.0±353.69 | 357.33±294.5 | 497.00±362.8 | 261.00±182.11 | <0.001 |
| hsCRP (mg/l)        | 20.04±10.08 | 14.83±9.9  | 22.10±8.37 | 22.16±20.04 | 0.089 |
| IL-5 (pg/ml)        | 16.45±11.34 | 12.34±7.34 | 11.74±5.62 | 11.32±4.19 | 0.008 |
| IL-8 (pg/ml)        | 72.39±153.21 | 31.86±53.21 | 254.90±405.52 | 63.00±54.38 | 0.003 |
| IL-6 (pg/ml)        | 3.21±5.06   | 3.16±4.46  | 3.64±6.58  | 16.95±46.79 | 0.420 |
| IL-13 (pg/ml)       | 10.03±40.67 | 1.85±3.65  | 1.88±1.75  | 3.26±5.98  | 0.420 |
| IL-17 (pg/ml)       | 8.25±16.67  | 9.65±10.20 | 5.81±3.89  | 7.18±5.35  | 0.411 |
| IL-33 (pg/ml)       | 32.22±29.01 | 18.53±13.92 | 38.51±34.69 | 30.68±27.89 | 0.090 |

SD: Standard deviation, BMI: Body mass index, SGRQ: St. George’s Respiratory Questionnaire, AQLQ: Asthma Quality of Life Questionnaire, FEV1: Forced expiratory volume in 1 s, hsCRP: Highly sensitive C-reactive protein, IL: Interleukin, FeNO: Fractional exhaled nitric oxide, AEC: Absolute eosinophil count, BA: Bronchial asthma
among various asthma phenotypes. Majority of the patients (70%–90%) in BA and BA-rhinitis phenotypes are in intermittent and mild persistent severity, while most of patients (67%–100%) in BA-obesity and BA-smoker phenotypes are in moderate-to-severe persistent severity. It is the mildest form in BA-rhinitis phenotype and worse severe in BA-smoker phenotype. A similar finding of severity of asthma more severe in obese asthmatic was also shown by Michelson et al. in a retrospective cohort analysis of the National Health and Nutrition Examination Survey 2001–2002 and 2003–2004. Another study also found that elderly asthmatics of BA-smoker phenotype have a more severe form of disease and neutrophilic inflammation. In the present study, SGRQ and MINI-Asthma Juniper Questionnaire were used to assess the quality of life. Both the above questionnaires showed that quality of life was worse in BA-smoker followed by BA-obesity phenotype, while it was better in BA-rhinitis and BA phenotypes. A study of 200 adult asthmatics by Maelje et al. also found that obesity is associated with poor asthma-related quality of life. Another study also found that smoking causes poor quality of life in asthmatics. Elkholy et al. showed that allergic rhinitis does not seem to further impair quality of life in subjects with asthma. All the above findings from different parts of the world are similar to our study finding that severity of asthma and quality of life are better in BA-rhinitis and BA than BA-obesity and BA-smoker phenotypes.

The atopic or allergic asthma is associated with an increased level of allergen SPT sensitivity and allergic inflammatory marker like FeNO. This type of patients is a better response to allergen immunotherapy and biological treatment. The present study showed a statistically significant different atopic status among the various asthma phenotypes ($P < 0.001$). The SPT sensitivity was highest among BA-rhinitis followed by BA-obesity and BA-smoker and least with BA. Among the common aeroallergens, the maximum positivity in overall asthma patients was against insects and HDM. In a study by Boulay and Boulet it was reported that the association between sensitization to specific allergens and airway hyperresponsiveness was strongest for indoor allergen such as HDM. Allergen exposure can increase airway responsiveness in nonasthmatic subjects with allergic rhinitis and is associated with an increase in markers of lower airway inflammation, particularly with indoor allergens and exposure to domestic animals, a farming environment, and passive smoking.

A study from the USA showed a positive association between the presence of obesity and the risk of atopic asthma.

### Table 2: The correlation of forced expiratory volume in 1 s with different inflammatory markers

| Marker   | $r$  | $P$    |
|----------|------|--------|
| hsCRP    | −0.134 | 0.145  |
| IL-5     | 0.277  | 0.002  |
| IL-6     | −0.063 | 0.494  |
| IL-8     | −0.179 | 0.050  |
| IL-13    | 0.108  | 0.240  |
| IL-17    | −0.117 | 0.203  |
| IL-33    | −0.006 | 0.948  |
| Vitamin D| −0.146 | 0.112  |
| ACE      | 0.009  | 0.922  |
| FeNO     | 0.176  | 0.050  |

FEV1 showed a significant correlation with IL-5, IL-8, and FeNO. IL: Interleukin, FeNO: Fractional exhaled nitric oxide, ACE: Absolute eosinophil count, FEV1: Forced expiratory volume in 1 s, hsCRP: Highly sensitive C-reactive protein
earlier studies had shown that the relationship between obesity and asthma is stronger in nonatopic individuals. The present study also found that FeNO level was highest in BA-rhinitis phenotype with a mean value of 45 ppb, and lowest in BA-smoker phenotype with a mean value of 25 ppb. Overall, there is no strict normal value of FeNO.

Different studies had shown different values in asthmatic and normal individuals. There is a considerable overlap of mean FeNO levels in healthy and stable asthma. As per ATS clinical practice guideline, FeNO is considered low when level of <25 ppb and high when level of <50 ppb in adult population. The high value is a marker of eosinophilic inflammation, and in symptomatic patients, responsiveness to corticosteroids is more likely. Kalpaklioglu and Kalkan showed that rhinitis and comorbid asthma patients are responsible for increased FeNO, irrespective of atopy. Kumar and Gupta in a study from India also showed that FeNO level is more in atopic asthma and family history of atopic diseases patients. Jacinto et al. also showed that smoke exposure decreases FeNO level. Hence, FeNO level can be used to differentiate the BA-rhinitis phenotype from other asthma phenotypes and as a marker of response to treatment in this phenotypic asthma patients.

On spirometry, more than one-third of BA-rhinitis (46%) and BA (33%) phenotype patients showed no obstruction. The lung function severity was mild in majority of BA-rhinitis and BA phenotypes and moderate to severe in majority of BA-obesity and BA-smoker phenotype patients. The spirometry findings were statistically different among groups (P < 0.001). All the asthma patients enrolled in the study were showing significant postbronchodilator reversibility. It has been shown that the smoking in both active and passive forms has a negative influence on lung function. A moderate-to-heavy smokers have more decline in lung function compared to never smokers of 15ml/year.

The E/L and E/N ratios were highest in BA-rhinitis phenotype and lowest in BA-smokers, and the ratio was statistically significant among groups (P < 0.001). The neutrophil/lymphocyte (N/L) ratio was not statistically significant among groups. Zhang et al. in a study found that the blood E/L, E/N, and eosinophil/monocyte (E/M) ratios were significantly higher in eosinophilic and mixed granulocytic asthma compared with neutrophilic asthma and also showed that the blood eosinophil ratios (E/L, E/N, and E/M) were also as efficient as blood eosinophil count to detect sputum eosinophilia. While blood neutrophil counts and N/L are poorly related to sputum neutrophil percentages, and have less utility. In the present study, it has shown a statistically significant difference in AEC among the different asthma phenotypes. We found the highest level in BA-rhinitis (mean = 586 cells) and lowest in smokers (mean = 278 cells). In line with the present study, Sunyer et al. showed that AEC was decreased in smokers disproportionately to the increase in total white cell count and the level was higher in rhinitis and obese asthmatics. Another study also showed that obese individuals with severe asthma have elevated serum eosinophils and high IL-5 levels, although obesity is typically associated with low sputum eosinophil and low exhaled nitric oxide levels. Similarly, Mathur et al. also support that greater eosinophil counts were seen in subjects with asthma alone and asthma with allergic rhinitis, identifying such patients with high eosinophil counts may benefit from the targeted therapeutics. The Vitamin D level in this study was not statistically significant among the asthma phenotypes (P = 0.108). However, the mean value of Vitamin D was below normal in all the asthmatic groups except BA-smokers where it was within normal limits. The overall mean value was 29.47ng/dl. Ali and Nanji in a review reported that the incidence of Vitamin D deficiency is high worldwide with almost half of the healthy people. The prevalence ranges from 69% to 82% in Indian population. The high prevalence of Vitamin D deficiency in asthma patients may be explained by overall deficiency in general population. Jiang et al. in a study of Chinese population showed that the current smokers had lower Vitamin D than never smokers. They found a greater number of cigarettes/day, and a longer smoking duration being associated with lower Vitamin D. These different findings may be due to genetic and lower pack-year smoker in the present study. Similarly, hsCRP was also not statistically significant among different asthma phenotypes. The overall mean value was raised with a mean of 18.39 ± 11.0 mg/l. It was highest in asthmatic smokers and lowest in only asthma phenotype. Sigari and Ghasri in a study of 100 asthmatics also found high hsCRP in asthma patients.

Among various ILs in different asthma phenotypes, the level of IL-5 and IL-13 was highest in BA-rhinitis phenotype. The IL-6 and IL-33 were highest in BA-smoker phenotype, while IL-8 was highest in BA-obesity and IL-17 in BA phenotype patients. Out of measured ILs, IL-5 and IL-8 showed a statistically significant P value in different asthma phenotypes. The mean value of IL-5 was highest in BA-rhinitis (16.45 ± 11.34) and lowest in BA-smoker (11.32 ± 4.19), while the mean value of IL-8 was highest in BA-obesity (254 ± 405.52) and lowest in asthma phenotype (31.86 ± 53.21). Krisiukeniene et al. in a study found that the IL-5 levels in the serum and
sputum of asthmatic never-smokers were significantly higher than that of asthmatic smokers.\[^{33}\] Another study by Liu et al. showed enhanced levels of IL-4, IL-13, IL-5, IL-6, IL-8, and vascular endothelial growth factor in serum and nasal lavage of AR children with asthma compared with control.\[^{34}\] Schmidt et al. in a study revealed the obese group had significantly elevated serum concentrations of IL-5, IL-12, and IL-13 compared to nonobese.\[^{35}\] Hasan and Ibrahim in a study asthmatic patients of Iraq found that the level of IL-8 level was significantly increase in asthmatic patients than healthy controls with a significant association and positive correlation to BMI.\[^{36}\] We also found a significantly positive correlation of IL-5 and FeNO with FEV1, while IL-8 showed a significantly negative correlation. Similarly, Hosoki et al. in a study showed that the BAL IL-8 level can distinguish controlled asthma from uncontrolled asthma and it negatively correlated with FEV.\[^{37}\] Another recent study by Nguyen and Chavannes found that the FeNO was significantly inversely correlated with the asthma control test score (r = −0.224, P < 0.001), and with spirometry, parameters indicate airway obstruction such as predicted FEV1 (r = −0.187, P < 0.05). They concluded that FeNO measurement is simple, noninvasive, and easy to interpret, so it can be a useful tool for asthma management in clinical practice.\[^{38}\]

**CONCLUSION**

The BA-rhinitis and BA phenotypes are younger, mild severe disease, having higher SPT positivity, milder spirometric values, and higher FeNO level than those of BA-obesity and BA-smoker phenotypes. The various measured serum biomarkers are different among asthma phenotypes. However, the IL-5, IL-8, and FeNO showed a significant difference among various phenotypes. The IL-5 and FeNO positively correlated while IL-8 negatively correlated with FEV1. We advise to the phenotypic classification of asthma patients whenever possible for better management options and better quality of life.

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**Conflicts of interest**

There are no conflicts of interest.

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