Inflammatory markers like C-reactive protein (hs-CRP) levels and exhaled breath nitric oxide (FE\textsubscript{NO}) levels are strongly and independently associated with respiratory impairment and more frequently bronchial hyper-responsiveness.\[3,4\] Thus, suggesting that both respiratory impairment and bronchial hyper-responsiveness are associated with a systemic inflammatory process. Obesity aggravates inflammation in asthma leading to increased severity of asthma and decreased responsiveness to the treatment, thus leading to increased morbidity and mortality in obese asthmatics compared to non-obese asthma patients.

Studies have established differential expression of inflammatory genes including cytokines, chemokines, complement proteins collectively termed as adipokines, in the adipose tissue of obese in comparison to lean human beings.\[5,6\] The current hypothesis is that this inflammation spills over into the blood, leading to inflammatory activation at sites distant to the adipose tissue. Adipokines like IL-6, TNF-\(\alpha\), plasminogen activator inhibitor 1, eotaxin,
vascular endothelial growth factor (VEGF) and monocyte chemotactic protein (MCP)-1 have been independently associated with inflammation in bronchial asthma and thus could be a link between obesity and asthma.\(^7\)

Hence, this study was undertaken to compare the pulmonary function parameters, atopic profile and inflammatory markers in obese and non-obese asthmatic patients of Indian population.

**MATERIALS AND METHODS**

**Study design and demographics**

The diagnosed patients of bronchial asthma (BA) as per Global Initiative For Asthma (GINA) guidelines\(^8\) were enrolled for the study from the outpatient clinics. A total of 60 subjects (30 females and 30 males) aged between 20 and 50 years were evaluated and they were divided into two groups using BMI classification.\(^9\) Group 1 had 30 patients (14 males and 16 females) with BMI < 25.0 kg/m\(^2\) and Group 2 had 30 patients (7 males and 23 females) with BMI > 30.0 kg/m\(^2\). The exclusion criterion were 1) Smoker (Former and current smokers) 2) Inhaled/oral steroid intake in preceding 1 month 3) Current medications for obesity/hypertension/ diabetes mellitus/CAD and 4) Unable to satisfactorily perform the nitric oxide maneuver. All the 60 subjects underwent a battery of investigations including pulmonary function test with diffusion capacity, blood sampling for lipid profile, skin prick tests, hs-CRP and FE\(_{NO}\) level measurements.

All subjects gave a written informed consent to participate in the study. The study protocol was approved by institutional ethical committee.

**Pulmonary function test (PFT)**

PFT was performed on a dry, rolling-seal spirometer of the Benchmark model lung function machine (PK. Morgan, Kent, UK). Maximal Expiratory Flow Volume curves were obtained as per the ATS recommendations.\(^10\) Dynamic lung volumes like forced vital capacity (FVC) and forced expiratory volume (FEV\(_1\)) was measured and static (or absolute) lung volumes like forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV\(_{1}\)) were measured as per guidelines.\(^10\) The diffusion capacity of the lungs was measured using the single-breath (SB) method (SBDL\(_{CO}\)). The gas used to calculate TLC was helium and the exhaled carbon monoxide was used to calculate the amount of carbon monoxide transferred to the blood.

**Skin prick testing**

Skin prick testing (SPT) to common aeroallergens and food allergens was performed in all the patients as per standard guidelines.\(^11\) Atopy was defined as a positive SPT (wheal diameter of > 3 mm as compared to buffer saline as control) for at least ≥1 aeroallergen.\(^11\)

**hs-CRP and FE\(_{NO}\) level measurement**

The hs-CRP levels were estimated by ELISA method using the ACCUBIND automated analyzer. The mean absorbance value for each set of reference standards, controls and samples were calculated. The absorbance for serum reference was plotted (y-axis) versus the corresponding CRP concentration (x-axis) in mg/ml on linear graph. The values of patient sample obtained were multiplied by the dilution factor of 100 to obtain CRP results in mg/L. The expected range of values of CRP, based on literature the expected values for adult serum sample is 0.068-8.2 mg/L. The measurement of exhaled nitric oxide was performed using single breath exhaled NO analysis (online method) on breath analyzer CLD 88 SP (M3014) chemiluminescence analyzer in accordance with the 2005 ATS/ERS recommendations.\(^12\)

**Lipid profile**

Triglycerides (TG), HDL, LDL, VLDL and cholesterol were estimated on the early morning fasting blood sample using standardized Bayer diagnostic kits. LDL were derived from these values using following formula:

\[
LDL = (Total\ cholesterol)-(HDL\ cholesterol)-(TG)/5
\]

**Statistical analysis**

Statistical analysis was done using SPSS 14.0 version and Graph pad 5.03 versions. The data were presented as mean ± standard deviation (SD). The differences in the mean baseline values of various measurements among group 1 and 2 was done by using Student’s t-test. The correlation between any two parameters between the groups or within the same group was made by using Pearson’s correlation coefficient. A p-value of < 0.05 was considered significant.

**RESULTS**

The demographic characteristics of both the groups are shown in Table 1. Of the total 60 subjects, 30 were males and rest 30 were females. Overall there were 51 atopic and 9 non-atopic patients in the study. Out of 60 patients, 30 were bronchial asthma patients with normal weight constituting group 1 and remaining 30 were obese bronchial asthma patients constituting group 2 as described earlier.

**Anthropometric variables**

The mean levels of the anthropometric variables have been described in Table 1. The weight (P = 0.001) and BMI (P = 0.001) showed statistically significant difference between the two groups; however, the age and height did not show statistical difference.

**Pulmonary function test**

The mean levels of PFT parameters in both the groups are depicted in Table 2. The levels of forced expiratory volume in 1 second (FEV\(_1\)), forced vital capacity (FVC), FEV\(_1\)/FVC ratio, forced expiratory flow at 25-75% (FEF\(_{25-75}\)), peak expiratory flow rate (PEFR) and forced expiratory time (FET) did not show significant difference between the two groups. On comparison of lung volumes, group 2 had lower levels of functional residual capacity (FRC) and expiratory reserve volume (ERV); the difference
being statistically significant ($P = 0.009$ and $P = 0.0002$, respectively). The residual volume/total lung capacity (RV/TLC) ratio was statistically higher in group 2 in comparison to group 1 ($P = 0.034$). Other parameters of lung volumes i.e., slow vital capacity (SVC), inspiratory capacity (IC), RV and TLC did not show statistical difference between two groups. The comparison of diffusion capacity, alveolar volumes and their ratio also did not show statistical difference.

### Atopic profile

The difference in atopic profile between obese ($n = 26$) and normal BMI ($n = 25$) asthmatic individuals for common Aero-allergen was not statistically significant ($P = 0.422$). Similarly, on analysis of SPT positive for food allergens the $P$-value that derived for this variable between obese ($n = 25$) and normal BMI ($n = 21$) groups is not in terms of statistical significance ($P = 0.293$).

### Inflammatory markers

The mean levels of exhaled breath analysis of FE$_{NO}$ in group 1 was $63.20 \pm 32.87$ ppb and in group 2 was $63.76 \pm 32.14$ ppb; the difference being statistically insignificant ($P = 0.9474$) [Table 1]. The mean hs-CRP level for the group 1 was $3.014 \pm 2.711$ mg/L and for the group 2 was $4.06 \pm 2.833$ mg/L. The difference was not in terms of statistical significance ($P = 0.1460$) [Table 1].

### Lipid profile

The mean value of lipid profile between the groups has been described in Table 1. The mean value of triglycerides, total cholesterol, VLDL and LDL did not differ significantly ($P = 0.71; 0.59; 0.47$ and $0.15$, respectively). However, the HDL levels were lower in group 2, the difference being statistically significant ($P = 0.03$).
DISCUSSION

Asthma and obesity are growing epidemics in the developing and the developed world. Asthma-obesity curve is J shape, the prevalence increases at both extremes of BMI. These results have been uniformly shown not only in western population but also in Chinese and Indian population. Studies have shown a significant positive association between increasing obesity (usually BMI) and a new diagnosis of asthma. The factors influencing the development and expression of asthma broadly divides into host and environmental, among which the host factors that includes are genetically predisposing genes to atopy and airway hyper-responsiveness, obesity and sex. Obesity is a systemic pro-inflammatory state associated with increased levels of inflammatory markers. Obesity affects the respiratory system via mass loading of the thorax, resulting in a reduction in chest wall compliance and changes in airway resistance. However; it is to be yet determined whether systemic or pulmonary inflammation has a role in development of asthma in patients with obesity.

The aim of current study was to compare the PFT parameters, levels of inflammatory markers (FE_{NO}, and hs-CRP), serum levels of lipid and sugar profile and atopic profile of common aero-allergen and food allergen between bronchial asthma patient with BMI < 25 kg/m^2 and obese bronchial asthma patient i.e., BMI > 30 kg/m^2.

In present study we have demonstrated that group with BMI > 30 kg/m^2 i.e., obese group had significant decrease in FRC and ERV in comparison to normal BMI group. This finding is consistent with previous studies The plausible explanation for this is increase in intra-abdominal pressure on the diaphragm and in fat mass on the chest wall leading to mass loading of the thorax, thus increases the deflationary pressure and reducing the compliance of lung and the respiratory system resulting in a reduction in functional residual capacity (FRC). Also, the mechanistic effects of obesity on lungs could lead to alteration in contractility of airway smooth muscles either by plastic adaptation to a shorter length or alterations in cross-bridge cycling resulting in an increase in airway responsiveness.

In a study by Jones et al. at a body mass index (BMI) of 30 kg/m^2, FRC and ERV were only 75% and 47%, respectively; of the values for a person with a BMI of 20 kg/m^2. However, other dynamic lung volumes including VC and total lung capacity (TLC) are often normal in obese individuals. Similarly, in current study these volumes were within 95% confidence limits for the predicted values.

The obese patient may show a normal, reduced or even increased FEV/FVC ratio. In mild obesity (percent of ideal body weight >120% but <150% or BMI >27.8 kg/m^2 but <31.1 kg/m^2), results of spirometry might be normal or might suggest a restrictive process, with a symmetric reduction in FEV, and FVC. Lazarus et al. in his study showed in obesity that there is a disproportionate reduction in FVC, demonstrating body mass index is significantly associated with the FEV/FVC ratio. In contrast, individuals with extreme obesity can demonstrate airflow limitation on spirometry. In current study, the FEV/FVC ratio in obese group was 71.40 ± 2.04%, thus showing a reduced ratio, however the difference with non-obese group was non-significant. In a comparative study of obese and non-obese asthmatics, Scott et al. reported no significant difference in FEV/FVC ratio between the two groups (68.5 vs. 72.0). The mechanism for the above-mentioned findings may be related to small airway collapse due to decreased lung volumes with increasing obesity or it may be independent. The mechanism of the small airway collapsibility has been related to the lower content of collagen in small airways, greater inflammation in the outer wall in comparison to the inner wall and inflammation of peribronchiolar region.

In current study, we did not found significant difference in atopic profile of normal BMI and obese bronchial asthma patients. A study by Scott et al. also did not found significant difference of allergic sensitization between obese and non-obese asthmatics (66% vs. 73.5%). In another study by Simard et al. reported the prevalence of atopy in obese asthmatics to be similar to that found in the general population. However, there are few reports of cross-sectional data showing a relationship between BMI and an increase in skin test reactivity. The results from current study did not show significant difference in positive reactivity to food allergens between both the groups. In a study by Ozol asthma developed in about 5% of individuals who suffer from food allergy and current asthma was reportedly triggered by foods among 6–8% of children and 2% of adults. However, the causal relationship between obesity and atopy is yet to be ascertained.

The National Cooperative Inner City Asthma Study reported children with sensitization to foods had increased asthma morbidity, with higher rate of asthma hospitalization and higher requirement of steroid medications. Similarly, the National Health and Nutrition Examination Survey data demonstrated that patients with asthma and food allergy are more likely to have a severe asthma exacerbation as compared to asthmatics without evidence of food allergy (OR = 6.9, 95% CI 2.4–19.7). Thus, for total asthma control and for better quality of life, steps should be taken to avoid foods in cases of food allergy.

Obesity is associated with increased plasma hs-CRP levels, which may be due to presence of adipocyte-derived interleukin-6. hs-CRP is also associated with degree of airway inflammation and airflow obstruction, serves as surrogate marker of this condition. Scott et al. reported elevated CRP levels in obese subjects in comparison to non-obese subjects. The study identified significant interaction between obesity and asthma on CRP and stated that the presence of asthma further increased CRP levels.
(P = 0.013). Simultaneously, significantly raised level of IL-6 was observed was in obese asthma compared to non-obese asthma group (p < 0.0001). Serum levels of hs-CRP correlate with BMI across the broad range of obesity.\[40\] Both the overweight (BMI, 25–29.9 kg/m²) and obese (BMI, ≥30 kg/m²) persons were more likely to have increased CRP levels than their normal-weight counterparts (BMI, <25 kg/m²), more so on obese women.\[41\] In current study, the obese group also had higher hs-CRP levels in comparison to normal group, though the results failed to reach statistical significance.

Exhaled nitric oxide (\(\text{FeNO}_3\)) measurement is a relatively simple, non-invasive and well-tolerated method and is frequently used as a clinical biomarker for assessment of airway inflammation.\[44\] Giugliano et al. showed that large excess of body weight might be associated to abnormalities of respiratory NO levels, as an impaired systemic NO production has been reported in obese with a sub-clinical low grade inflammation or by interacting with changes in conducting airway and lung volumes.\[45\] However, in current study the \(\text{FeNO}_3\) levels did not show significant difference between obese and non-obese groups.

Hypercholesterolemia increase the risk of asthma by promoting similar pro-inflammatory mediator in the airway, and its effect on asthma is independent of obesity.\[46\] In current study, the mean levels of triglycerides, total cholesterol, VLDL and LDL were more in the obese group but the difference was not statistically significant. The statistically significantly lower value of HDL in obese group suggests that there is a role of lipids in the inflammation of the disease. In a study by Fessler et al.,\[47\] asthma was inversely related to serum total cholesterol and non HDL-cholesterol, reflecting a relationship between cholesterol and the inflammation of asthma.

**CONCLUSION**

In current study of Indian population, there were no significant difference in between the groups for inflammatory markers like \(\text{FeNO}_3\) and hs-CRP, skin testing to common aeroallergens and food allergens as consistent with the western data. The parameters like FRC and ERV in the obese group also had higher \(\text{FeNO}_3\) levels in comparison to normal group, though the results failed to reach statistical significance.

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