An Observational Study to Assess the Prevalence and Impact of Obesity in Asthma Management

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ABSTRACT

Objectives: To assess the prevalence of obesity among asthmatic patients and their clinical profile to the treatment there by managing asthma among obese patients and to evaluate sex differences in the relationship between asthma and obesity in adult asthmatic patients.

Methodology: A prospective study was conducted among the outpatients of pulmonology department for a period of 6 months duration in a tertiary care referral hospital. 100 asthmatic patients above 18 years of age were enrolled from Malabar region of Kerala, India in order to evaluate the effectiveness of pharmacist intervention in reducing the asthma severity. Exacerbation and NO: of hospitalization. Results: The total number of patients involved in the study was 100. Out of these 37% was found to be obese (class I and class II). Fischer’s exact test was performed and p value was found to be <0.01 that shows there is a significant difference in PFR between obese and non-obese asthmatic patients. Nearly two-fifth of the non-obese patients suffering from asthma had improvement, where as one-third of the obese patients with asthma had no improvement. 70% of the study population had poor lung function (FEV1/FVC) < 0.75 and 30% of the study population had normal lung function (FEV1 ≥ 0.75). Conclusion: In conclusion, our prospective study provides the first evidence demonstrating an association between obesity and asthma in adult male and female patient. Elevated BMI, particularly obesity is associated with subsequent poor asthma control, especially in the risk domain (exacerbation). These findings further support the importance of facilitating weight loss in overweight and obese adults with asthma. The incidence of both obesity and obesity conditions has been increasing and they share common risk factors. Obesity and asthma due to its unique relation has emerged as a different phenotype of asthma.

Key words: Asthma, Obesity, Prevalence, Exacerbation, Gina criteria, Act score.

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INTRODUCTION

In recent decades, asthma and obesity have increased markedly in many countries. This situation represents a public health problem due to the probability of an early death in a large number of individuals.1 The World Health Organization (WHO) includes both conditions among the principal chronic diseases. To establish the diagnosis of overweight and obesity in clinical practice, one of the most accessible and practical indexes to estimate excess fat is the body mass index (BMI), which is the value of weight (in kg) divided by the value of height (meters) squared. Asthma is a chronic inflammatory disorder of the airways involving many cells and elements (adipose, eosinophils, neutrophils, lymphocytes, macrophages and epithelial cells) that cause recurrent episodes of nocturnal predominance cough, wheezing, difficulty breathing and a sensation of chest tightness. These symptoms are usually associated with a large but variable bronchial obstruction, which is often reversible either spontaneously or with treatment.2

A variety of reported observations suggest that obesity might impact the lung in multiple ways.3 Moreover, studies report that individuals with persistent asthma are significantly limited in the practice of physical activity, thus reducing energy expenditure, a fact that contributes to the growing increase in the prevalence of overweight and obesity. Like-wise, obesity seems to have negative impact on the level of asthma control.4

Lessard et al. showed that obese individuals are more likely to have not controlled asthma when compared to non-obese.5

Obesity is one of the biggest health problems in the world. It acts as a risk factor for a multiple number of diseases which includes diabetes, cardiovascular disease, stroke, cancer, dementia and various others. Obesity is caused eating too much, moving too little. If you consume high amounts of energy particularly fats and sugars but don’t burn of the energy through exercise and physical activity, much of the surplus energy will be stored by body as fat. Obesity is a risk factor for asthma in multiple demographic groups. Female gender is significantly associated with asthma and obesity.

With increasing urbanization, mechanization of jobs and transportation, availability of processed and fast foods, dependence on television for leisure, people are fast adopting less physically active lifestyles and consuming more energy dense, nutrients poor diet. As a result, overweight and obesity and associated chronic health problems such as diabetes, hypertension, cardiovascular diseases and cancer are increasing rapidly particularly among middle class, urban population. Obesity promotes a systemic inflammatory condition which paved the way to increase of asthma severity and its poor control. The prevalence of asthma is around 300 million and is expected to increase another 100 million by 2025. Obesity on the other hand, also effects a large number of individuals.

Overweight in an adult is defined as BMI between 25 to 30 kg/m² and obesity when the BMI >30 kg/m². The association between obesity and asthma has been suggested by an increase in Body of literature. Many investigators have interpreted the data suggesting that obesity both
increases the risk of incident asthma and alters prevalent asthma toward a more difficult-to-control phenotype. Moreover, seems to have negative impact on the level of asthma control.

Asthma control is defined in terms of both impairment and risk. Impairment is the frequency and intensity of symptoms as well as the functional limitations a person experiences. It is measured using various validated questionnaires such as the Asthma Control Test (ACT) or the Asthma Control Questionnaire (ACQ). Risk is determined by the possibility of future adverse events such as exacerbations and hospitalizations. Severity can refer to a spectrum of findings including loss of function of the organs from asthma or to the occurrence of severe acute exacerbations.

The prevalence of asthma is higher in obese than in lean adults and obesity increases the incidence of asthma by 2.0-and 2.3 fold in children and adults and also significant dose dependent effects of elevated body mass index on asthma are observed. Obese asthmatic patients are often described as severe and poorly controlled as they are less responsive to corticosteroids and exhibit a different inflammatory phenotype. Obesity is associated with chronic low-grade systemic inflammation that is thought to enhance systemic complication. In many observations, a number of epidemiological study indicate that obesity increases the risk of developing asthma and implicates immunological mechanism relevant to both disorders.

BMI has been commonly used as an indicator of adiposity in asthma studies because it is relatively easy and inexpensive to obtain. However, BMI does not differentiate between lean mass and fat mass. Girls have greater body fat than boys at the same level of BMI. In adults BMI correlates better with lean mass in male subjects, whereas in female subjects it correlates better with fat mass. Furthermore, Daniels et al. found that the relationship between BMI and body fat was dependent on maturation stage, race, sex and waist/hip ratio in adolescents. In part, these limitations with BMI might explain the observation in larger epidemiologic studies of the effect of obesity on asthma in female but not male subjects. Therefore, more direct measurements of body fat might provide greater insight into the relationship between obesity and asthma.

**METHODOLOGY**

The study was carried out in Malabar region of Kerala, India. A prospective study conducted among the outpatients of pulmonology department of tertiary care referral hospital. The study was divided into three phases. In phase I, all the relevant information were collected from patient case file, pulmonary function test values. The data were analyzed, evaluated, categorized and recorded in a documentation form. In Phase II, the patients were categorized as Underweight, overweight and obese according to International classification of BMI. Number of hospitalization and Number of exacerbation was monitored. All the patients were provided with proper counseling and leaflet was distributed. In phase III, review was carried out in patients who were enrolled in phase I and the pulmonary function test were repeated and comparison was performed with the pulmonary function test value in the Phase I. Study was carried out for a period from December 2017 to May 2018 among the outpatients of Pulmonology department. This study was approved by the ethical committee of the institution and an official consent was also given for the purpose of performing the study. It was certified by the Institutional Ethics Committee (IEC) and approved the proposal of the study. An observational study was conducted. The PFT value of asthmatic patients including PFR reading, patient details and previous medical history under the Pulmonology department were analyzed during the study period and an inclusion and exclusion criteria was made. The inclusion and exclusion criteria as specified in the protocol submitted to IEC and approved by IEC of KIMS AL SHIFA Hospital. Patients above 18 years are diagnosed to have asthma by pulmonary function test in accordance with GINA CRITERIA, patients diagnosed with symptoms of airflow obstruction were enrolled in the study. Patients those who are having asthma- COPD overlap, patients those who are diagnosed to have asthma with smoking habit, patients below 18 years, patients who are diagnosed with tuberculosis, patients with known malignancies were excluded from the study.

Lithiums supporting the study were collected from authorized international and national journal. Information from the review of these literatures and the scenario in the study site were put together in developing a data collection form and a protocol. A data collection form, pulmonary function test, Peak flow meter, lexici BMI calculator, leaflet, Asthma control Test according to GINA criteria, Asthma severity classification based on GINA criteria.

A patient detailed data collection form, Asthma control test according to GINA criteria and also include a questionnaire form based on the asthma severity, PFT values based on Spirometry and PFR reading of each asthmatic patients. These are the important documentation form was designed to collect information necessary for this study. PFR reading is taken at first review. Patient data collection form includes the following details. Patient Demographics: This gives a brief detail about the patient for example details like Name, Age and Sex etc. Patient related characteristics: It gives detailed about the medical record number (MRD NO), Department and co morbid condition Socio economic status: It includes the educational status, Occupation (student, Housewife/work)Pulmonary function test details: It gives the values of FEV1(L) and FVC (L) and its ratios in first consultation and review number of Hospitalization: It includes the no: of admission based on the asthma severity Response to treatment : It gives the result of the treatment. PFT is a non-invasive tests that show how well the lungs are working. It is a complete evaluation of respiratory system including patient history, physical examination and test of pulmonary function. The primary purpose of PFT is to identify the severity of pulmonary impairment. A peak flow meter is a small device that helps to check how well asthma is controlled and it determines the lung function by measuring the maximum range at which air is exhaled from the lungs. BMI was calculated using Lexi comp BMI calculator and classified the patients based on obese, overweight and underweight. BMI categorize the patient based on the values as follows Underweight = <18.5, Normal weight = 18.5-24.9, Overweight= 25-29.9, Obesity = BMI of 30 or greater. These calculations is a measure of body fat based on height and weight that applies to adult men and women. A leaflet consisting of information about asthma and its etiology, symptoms, prevention and treatment was prepared during phase I and handover to the asthmatic patients.

The asthma control test (ACT) as a predictor of GINA guideline-defined asthma control. It evaluates the asthma control test score based on the guidelines. The ACT is validated 5- item, patient completed measures of asthma control with a recall period of four weeks. An ACT score < 19 (not well controlled asthma),>20 predicted GINA defined controlled asthma. The ACT has the added advantages that it does not require lung function assessments and can be applied at all levels of health care. ACT questionnaire is a simple, self-administered AND rapidly completed assessment tool. Global Initiative for asthma (GINA) guidelines categorize asthma severity as four steps, step -1(intermittent), step-2 (mild persistent), step -3 (moderate persistent), step- 4(severe persistent). Patient at any level of severity- even intermittent asthma -can have severe attack. Severity is assessed prospectively from the level of treatment required to control and symptoms and exacerbation. A prospective study was conducted to determine the prevalence of asthma in obese patients. The sample was collected from the Pulmonology department during the outpatient consultation with physician. In the first visit the BMI of the each patients were calculated and then categorized according to International BMI.
classification. The PFT report were collected and FEV1, FVC, FEV1/FVC ratio were analyzed and documented.

Based on these PFT values patients were classified Underweight, Overweight, Obese (class-I, II and III) and all patients were provided with counseling and leaflet was distributed. On review improvement in lung function was evaluated by analyzing PFT parameters as well as PFR reading. By analyzing the PFT values, it is concluded that the improvement in lung function is less in obese when compared to non-obese patients and symptoms worsening is more in obese. These facts were put into notice of all the obese patients. The study was carried out in 3 phases:

An observational study was conducted for all patients who were found eligible according to the inclusion criteria. The duration of this phase was 3 months. All the relevant information were collected from patient case file, pulmonary function test values. The data were analyzed, evaluated, categorized and recorded in a documentation form. Duration of this phase was 1 Month. Based on the data recorded in the phase I, the patients were categorized as Underweight, overweight and obese according to International classification of BMI. Number of hospitalization and Number of exacerbation was monitored. All the patients were provided with proper counseling and leaflet was distributed. During this Phase, review was carried out in patients who were enrolled in phase I and the pulmonary function test were repeated and comparison was performed with the pulmonary function test value in the Phase I.

The PFR reading were estimated. Improvement in lung function were assessed by comparing pulmonary function test and Peak flow rate reading. Data was entered into Microsoft Excel and the recorded data were statistically analyzed using statistical package for social sciences (SPSS) software version 20.0 for WINDOWS. The collected data from subjects were analyzed by statistical treatment using appropriated statistical tools.

**RESULTS**

Of 100 patients greater than 18 years of age and older, the patients with age group between 40-50 (21%) were significantly higher when compared to other age groups [Figure 1]. The enrolled group with age group between 80-90 constituted only 1% and the mean age of the study participants were 50.8 (17.1).

Fischer’s exact test was performed and p value was found to be <0.01 that shows there was a significant difference in PFR between obese and non-obese asthmatic patients. Nearly two-fifth of the non-obese patients suffering from asthma showed improvement, whereas one-third of the obese patients with asthma showed no improvement. Among selected patients, female patients were significantly higher in number (63).

**As per WHO Classification**

Body Mass Index (BMI) of the patient = weight (kg) / Height (m2)

Only one-fifth of the participants had normal BMI status. Among the study population, 37% of the population belongs to obese group (class I and class II), 41% to overweight and 21% were normal weight patients [Table 1]. According to Body Mass Index (BMI) obese asthmatics have more frequent emergency visits, more hospitalization for asthma related complaints and increased missed work days. Mean serum level of C-reactive protein (CRP) and leptin was significantly correlated with asthma severity based on GINA classification [Figure 2] Nearly two third of the patients suffering from asthma were females and constituted 63% of the total study population. 70% of the study population had poor lung function (FEV 1/FVC) < 0.75 and based on the test scores, only one-fifth of the study participants have asthma well controlled. While comparing pre and post treatment, it has been found that the normal lung function of the study population has been significantly improved after patient counseling [Figure 3].

**Table 1: BMI status* of the study participants, N=100.**

<table>
<thead>
<tr>
<th>BMI status</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>Overweight</td>
<td>41</td>
<td>22</td>
</tr>
<tr>
<td>Obese</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Class I Obese</td>
<td>37</td>
<td>66.5</td>
</tr>
</tbody>
</table>

*As per WHO Classification.

Almost one-third of the patients suffering from asthma were obese. Only one-fifth of the participants had normal BMI status.

An ACT score <19 indicates not well controlled asthma and >20 predicted GINA defined controlled asthma [Table 2]. Compared to normal or underweight individuals, both obese and overweight patients have poor lung function. Based on the test scores, only one-fifth of the study participants have asthma well controlled.

While comparing pre and post treatment Figure 3, it has been found that the normal lung function of the study population has been significantly improved after patient counseling. 80% of the patients suffering from asthma did not have worsening of symptoms after treatment of 6 months.
Chandrasekhar, et al.: prevalence and impact of obesity in asthma management

The study results of 100 adult patients presenting with asthma at the pulmonology department demonstrated that 37% of the total population was obese. However, in comparison with normal-weight patients, obese patients with asthma exacerbation had a significantly high risk of hospitalization. Differences in study design, patient population, classification of BMI status, clinical setting and statistical power- or possible combination of these factor contribute to differences in different studies. Obesity in India is reported to be different from that of other countries. Several studies in India have shown that Indian population are at risk of obesity related comorbidities at a lower level of BMI and waist circumference than that recommended by WHO.

The patients with age group between 40-50 (21%) were significantly higher when compared to other age groups. The patients with age group between 80-90 constituted only 1%. Mean age of the study participants is 50.8 (17.1). Ho et al. evaluated more than 4000 participants between 20-25 years of age and found that subjects who were overweight had an increased odds of physician-diagnosed asthma (OR 1.75 95% CI 1.18-2.61) compared with those who were normal weight. Our study demonstrated that one-fifth of the participants in the age group of 40 to 50 years were largely diagnosed with obesity related asthma. National health and nutritional examination survey I (NHANES I) was an epidemiology follow-up study of 9456 participants and found a moderately increased risk for asthma development among obese adults aged 25-75 years.

Among selected patients, female patients were significantly higher in number. Nearly two third of the patients suffering from asthma are females and constituted 63% of the total study population. Although the exact mechanisms are unclear, estrogen affects lung function and inflammatory process via various pathways. It is hypothesized that estrogen in adipose tissue causes an early menarche in females and delayed puberty in males. In addition, it has been hypothesized that high serum leptin levels precede airway inflammation, an important asthma characteristic. Almost one-third of the patients suffering from asthma were obese. Only one-fifth of the participants had normal BMI status. Among the study population, 37% of the population belongs to class 1 obese, 1% belongs to obese group, 41% belongs to overweight and 21% were normal weight patients. It has been demonstrated that a positive relationship between BMI-SDS (Standard Deviation Score) and asthma in females but not in males. The role of estrogen, leptin, genes and epigenetics should be investigated, as these features might play an important role in the relationship between sex, asthma and BMI status.

Obesity causes a restrictive effect on the lungs. More reduction in lung volume was seen in overweight and mildly obese individuals. Compared with non-overweight subjects, obese Subjects with asthma were more likely to report continuous symptoms (B Taylor et al.). Huovine et al. showed that after a 9 year follow up of 9672 adult patients, obese participants had a substantially higher risk of asthma development than participants with a normal body mass index. Obesity is associated with a reduction in residual volume, functional residual capacity and expiratory reserve volume. Obesity also causes a reduction of both FEV1 and FVC with a preserved FEV1/FVC ratio. It has been found that subject with asthma poor obese were more likely to have lower FEV1 than their counter parts of normal weight. The blood level of C reactive protein and leptin which are two inflammatory markers, suggest that the systemic inflammation state in obese asthmatic is plausible mechanism that could explain the relationship between asthma and BMI. Weight reduction reduces closing capacity- that is dependent airways close later in expiration which tends to increase FEV in one second and the FVC. M. Peters. Golden et al. shown that asthma severity is significantly greater for individuals in the overweight and obese groups as shown by their lower FEV1 (% pred).

Pelegrino et al. studied 200 patients and reported 32% presented a BMI ≥ 30kg/m². Our study shown a reduction of both FEV1 and FVC with a preserved FEV1/FVC ratio. However previous studies yielded

Table 2: Asthma test score of the study participants, N=100.

<table>
<thead>
<tr>
<th>Asthma test score</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poorly controlled</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>Symptoms may not be well controlled</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td>Well controlled</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

Based on the test scores, only one-fifth of the study participants have asthma well controlled.
contradictory data on whether obesity effects respiratory function in asthmatic subjects. We found that subjects with asthma who were obese were more likely to have higher FEV1 than their counterparts of normal weight, despite similar level of asthma severity and control. One possible explanation for this finding was the more difficult control of the disease in obese patients, despite better pulmonary function, assessed by Spiro metric tests, when compared to non-obese patients.

60% of the selected patients was having peak flow reading less than the normal value. The normal value of peak flow rate is above 400. The peak expiratory flow also called peak expiratory flow rate is a person’s maximum speed of expiration as measured with a peak flow meter, a small, hand-held device used to monitor a person’s ability to breathe out air. The measuring peak flow using this meter is an important part of managing asthma symptoms and preventing asthma attack.

Pulmonary function was assessed with a computerized spirometer and Forced vital capacity (FVC), FEV1 and FEV1/FVC were measured. All parameters were reported as percent of predicted for age, height and gender. PEFR was measured using a portable peak flow monitor. The result was reported as percentage of the predicted for age, height and gender. We used GINA classification system to assess the disease severity according to the daily medication regimen, which divides patients into four severity categories (mild, intermittent; mild, moderate; severe and persistent asthma) based on frequency of symptoms, Spiro metric data and intensity of drug therapy. The multivariate analysis showed a significant correlation between obesity and worse asthma control using the GINA classification (OR 20; 95% CI 7.5 –53). The univariate analysis showed that obesity and overweight were associated with a higher GINA severity classification, lower GINA control classification and poorer quality of life (AQLQI score of more than 6). FEV1, FVC and FEV1/FVC ratio were significantly lower in the obese group.

The improvement in ACT score after treatment initiation and patient counseling was significantly higher when GINA approach was used. The number of patients who achieved asthma control at the follow up visit and required no treatment adjustment was found to be about 60% in these category. This study shows that the ACT was responsive to changes at the initiation of asthma treatment. It has also showed the usefulness of the ACT score for the initiation of asthma treatment. Despite ample amount of evidence that supports the use of the ACT for treatment adjustment, a unique feature of this study is the presentation of new evidence supporting the utilization of the ACT in making an initial asthma treatment decision.

Epidemiologic studies evaluating a number of risk factors and their association between obesity and poor asthma control. Schatz et al. used the ACT questionnaire to examine factors associated with asthma control in 570 patients aged 35 years and older enrolled in a large managed health care organizations. In a multiple linear regression analysis, a higher BMI was an independent predictor of poor asthma control (p<0.01). Lavoie in his study on 382 adults found that patients with higher BMI scored higher in asthma control questionnaire (ACQ) independent of their age and sex.

Our study demonstrated that obesity associated with asthma was modified by sex and history of allergy. A stronger association was found in women than in men AND in those with no allergy history than in those with allergy history. These findings are consistent with and may help to explain the observed differences in association of obesity and asthma in between men and women.

Furthermore, in the setting of obesity epidemic, the higher risk of hospitalization among obese patients ease of interest to policy makers and payers. To mitigate asthma related health care use in an already stressed health care system our finding should encourage policy makers to develop and evaluate public health intervention that promote weight reduction in this high-risk population.

In summary, the nature of the asthma- obesity relationship is very complex and involves several mechanisms, of which major roles are played by bronchial smooth muscle cells dysfunction, inflammatory mediators and oxidative stress, dietary and genetic factors.

Limitations

The sample size and the duration of the study were not having adequate power to detect the complete association of obesity with asthma and also in many cases the ACT score may have been under-estimated due to the lack of relevant data. During patient first review, conducting pulmonary function test have added to the economic burden of the patients and is the major limitation of our study. Also, the patients below 18 years of age, those with asthma- COPD overlap and those with known malignancies have been avoided due to time limitations.

CONCLUSION

In conclusion our prospective study provides an evidence demonstrating the prevalence of obesity in asthma. Elevated BMI, particularly obesity is associated with subsequent poor asthma control, especially in the risk domain (exacerbation). These findings further support the importance of facilitating weight loss in overweight and obese adults with asthma. The incidence of both asthma and obesity conditions has been increasing and they share common risk factors. Obesity and asthma due to its unique relation has emerged as a different phenotype of asthma. From a research prospective, newer studies are required in context of the new obesity classification in India, undiscovered issues and the relationship between obesity and asthma.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS


REFERENCES


