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Is Obesity and Gastro Esophageal Reflux Disease (GERD) Associated with Severe Asthma? – A Study of 181 Cases

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ABSTRACT

Background: *Around 5 – 10% of asthma patients have severe asthma .Severe asthma is considered as a distinct asthma phenotype. Identifying the risk factors, triggers and co morbid conditions associated with severity of asthma will help in further defining this phenotype and subsequent targeted interventions can help in better control of severe asthma. Obesity is not only known to be a risk factor for asthma but is also associated with severe asthma. A significant association has been found between Gastro esophageal reflux disease (GERD) and asthma. Symptomatic GERD is associated with poorly controlled asthma.*

Aims and objectives:

1. To study association between Obesity and Severe asthma.

2. To study association between GERD and Severe asthma.

Materials and Methods: *This was a case control study done on 181 bronchial asthma patients, attending Respiratory Medicine department of A.J. Institute of Medical Sciences, Mangalore. Detailed history including treatment history and clinical findings of every study subject was obtained and patients were asked peer reviewed, standard asthma related questionnaires.*

Each patient's Body Mass Index (BMI) was recorded. Diagnosis of GERD in study subjects was made based on classical symptoms of heartburn and regurgitation. Among the Study population, patients with severe asthma were identified as per GINA and American Thoracic Society recommendations. Data was compiled and statistical analysis was done using Chi-square test and P-value was calculated.

Results: *Total number of study population was 181, between the age group of 15 to 80 years. 113 (62.4%) were females and 68 (37.6%) were males. 95 patients (52.5%) were having severe asthma. Out of 14 (7.7%) underweight patients 4 (2.2%) had severe asthma. Out of 80 normal weight patients 23(44.2%) had severe asthma. Out of 42 (23.2%) overweight patients, 30 (16.6%) had severe asthma. Out of 45(24.9%) obese patients, 38 (21%) had severe asthma. Severe asthma was more common in overweight and obese patients than in underweight and normal weight patients which were statistically significant. Overweight and obesity was more common in females than in males, which was statistically significant. Total patients with GERD were 89 (49.2%). Out of 89 patients with GERD, 65 (35.9%) had severe asthma and amongst 92 patients without GERD, 30(16.6%) had severe asthma. Severe asthma was more common in patients with GERD which was statistically significant. GERD was more common in overweight and obese patients as compared to normal weight patients.*

Conclusions:

1. Severe asthma is more common in overweight and obese patients as compared to patients with normal BMI and is more common in females as compared to males.

2. Obesity is associated with higher incidence of GERD and Patients with GERD have higher incidence of severe asthma

KEYWORDS :

Introduction:

Asthma is now considered as spectrum of diseases with various phenotypes with different underlying disease processes and differences in severity and prognosis [1]. Around 5 – 10% of asthma patients have severe asthma .Severe asthma is considered as a distinct asthma phenotype [2, 3]. Severe asthma includes patients with 'Refractory asthma' or 'Treatment resistant asthma' in which patients with a confirmed diagnosis of asthma, whose symptoms or exacerbations remain poorly controlled despite high-dose inhaled Glucocorticosteroids plus a second controller such as Long acting beta 2 agonist (and / or systemic corticosteroids) and management of comorbidities, or whose asthma control deteriorates when this treatment is stepped down and in whom response to treatment of comorbidities is incomplete[1]. It is associated with very poor quality of life and increased morbidity and mortality[1-3].

Identifying the risk factors, triggers and comorbid conditions associated with severity of asthma will help in further defining this phenotype and subsequent targeted interventions can help in better control of severe asthma. Obesity is not only known to be a risk factor for asthma but is also associated with severe asthma [4, 5]. Weight reduction as therapeutic intervention has shown to improve asthma control in obese patients[6].

A significant association has been found between Gastro esophageal reflux disease (GERD) and asthma. Symptomatic GERD is associated with poorly controlled asthma[7, 8].

Aims and objectives:

1. To study association between Obesity and Severe asthma.
2. To study association between GERD and Severe asthma.

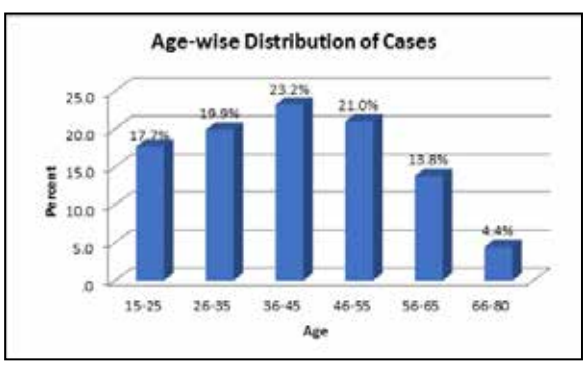
Materials and Methods:
This was a case control study done on 181 bronchial asthma patients, attending Respiratory Medicine department of A.J. Institute of Medical Sciences, Mangalore. Bronchial asthma was diagnosed as per GINA guidelines. Both male and female patients between age group 15 to 80 years were included in the study. Current or past Smokers, patients with a previous history of pulmonary tuberculosis or active tuberculosis, those with chest wall deformities, coexistent neuromuscular disorders, and cardiovascular diseases were excluded from the study.

Detailed history including treatment history and clinical findings of every study subject was obtained and patients were asked peer reviewed, standard asthma related questionnaires. Each patient's Body Mass Index (BMI) was recorded and patients were classified as per ICMR classification for BMI.<18.4 – underweight, 18.5-22.9 – normal, 23 – 24.9 – Overweight, > 25 – Obese. Diagnosis of GERD in study subjects was made based on classical symptoms of heartburn and regurgitation[9].

Among the Study population, patients with severe asthma were identified as per GINA and American Thoracic Society recommendations, depending on parameters like level of control of asthma, persistent symptoms despite optimum therapy, and use of high dose of inhaled steroids, frequent use of systemic corticosteroids, frequent exacerbations, frequent hospital admissions and Intensive Care Unit (ICU) admissions due to asthma[1, 3].

Data was compiled and statistical analysis was done using Chi-square test and P-value was calculated (P-value < 0.05 significant)

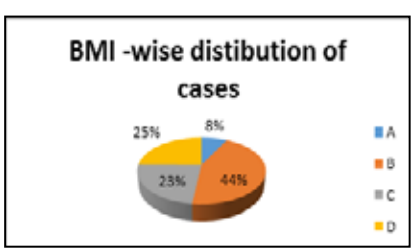
Results:
Total number of study population was 181, between the age group of 15 to 80 years, majority patients between 26 to 55 years of age.



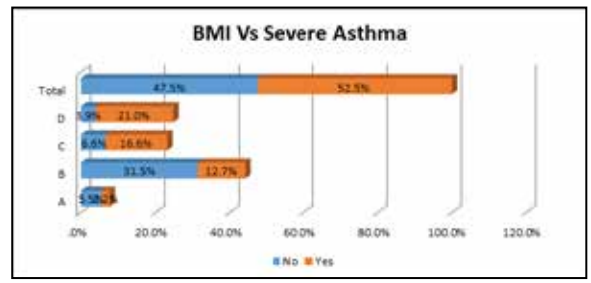
Graph showing age wise distribution of patients

Out of 181 patients, 113 (62.4%) were females and 68 (37.6%) were males. Out of 181 patients, 95 (52.5%) patients were having severe asthma and 86 patients (47.5%) did not have severe asthma.

A. Out of 14 (7.7%) underweight patients 4 (2.2%) had severe asth ma
B. Out of 80 normal weight patients 23(44.2%) had severe asthma.
C. Out of 42 (23.2%) overweight patients, 30 (16.6%) had severe asthma
D. Out of 45(24.9%) obese patients, 38 (21%) had severe asthma.
E. Severe asthma was more common in overweight and obese pa tients than in underweight and normal weight patients which were statistically significant.
F. Overweight and obesity was more common in females than in males, which was statistically significant.

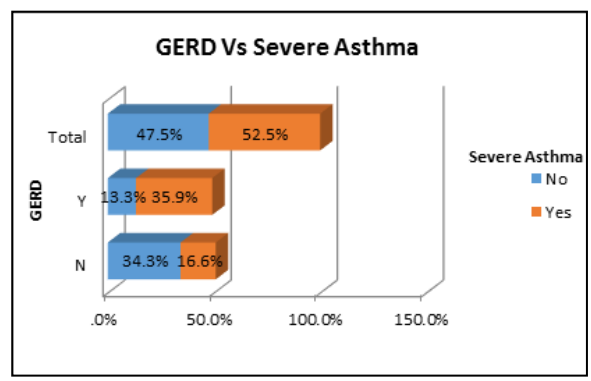


Graph showing BMI-wise distribution of cases



Graph showing comparison of prevalence of severe asthma among different BMI category.

Total patients with GERD were 89 (49.2%) and 92 patients had no clinical evidence of GERD. Out of 89 patients with GERD, 65 (35.9%) had severe asthma and amongst 92 patients without GERD, 30(16.6%) had severe asthma. Severe asthma was more common in patients with GERD which was statistically significant. GERD was more common in overweight and obese patients as compared to normal weight patients.



Graph showing comparison of prevalence of severe asthma between patients with and without GERD.

Discussion:
Our study showed that incidence of severe asthma was significantly higher in overweight and obese patients as compared to normal weight patients. Most of the epidemiologic studies indicate that obesity is not only associated with increased incidence and prevalence of asthma[4], but also associated with poor control and severity of asthma[5, 10]. ATS workshop in 2010 concluded that asthma in obese may represent a unique phenotype with more severe disease that does not respond to conventional therapy [11]. Youkou et al in his study of 3146 patients, in 2011 showed that obese asthmatics had more severe disease and higher utilization of inhaled salmeterol and leukotriene antagonists [12]. In a cross sectional study done by Andreina Bruno et al[13] on patients with severe asthma, obese patients had poor asthma control with increased number of exacerbations and use of high dose of steroids. In contrast, a study by J. Sastre et al [14] did not show positive relation between obesity and incident asthma and severity of asthma.

Obesity is characterized by chronic low grade systemic inflammation and persistence of this inflammation in airways or a different type of inflammation in the airways may be responsible for severity of asthma[15]. Obesity related increase in serum levels of pro-inflammatory TNF alpha, IL-6 and leptin or decrease in anti-inflammatory adiponectins are being studied as responsible factors for severe asthma in obese individuals [16].

Obesity associated co-morbidities such as obstructive sleep apnea syndrome and GERD and mechanical factors can contribute to severity. Obesity reduces pulmonary compliance, lung volumes especially FRC and ERV and diameter of peripheral airways, affects volume of blood in the lungs hence affecting ventilation perfusion relations [17, 18]. In addition to asthma severity, increased fat and general lack of fitness may contribute to dyspnea in obese individuals.

There is a possibility of common genetics involved in asthma and obesity and this is being extensively researched. Weight reduction has a therapeutic value in asthma control in obese patients and is shown to improve lung functions in obese patients [6]. Mauro Maniscalco et al in a study showed weight reduction improved respiratory symptoms, decreased rescue medication use and improved lung function [19].

Almost half of our asthma patients had GERD in our study. Studies have shown that patients with GERD have greater risk of asthma associated symptoms than general population. Patients with GERD are more likely to have concurrent asthma compared to patients without GERD [7, 8]. Treatment of symptomatic GERD improves level of control of asthma [20]. Prevalence of GERD in asthma patients has ranged from 25% to 80% in studies [9-11]. GERD was present in 38% of asthma patients in a study conducted by the American Lung Association Asthma Clinical Research Centers (ACRC) Network [20]. In our study, prevalence of severe asthma was more in patients with GERD than in patients without symptomatic GERD, which was statistically significant. This confirms earlier studies that symptomatic GERD is associated with severity of asthma. In a study by Emily Di Mango et al[20], patients with proximal reflux had significantly worse asthma control and health related quality of life despite no change in lung functions.

Some of the explanations given for association between GERD and asthma are a) Pressure changes in thorax of asthmatics allow more acid to reflux into esophagus. b) Asthma medications like beta 2 agonists may relax lower esophageal sphincter and cause GERD in asthma patients. c) Acid in esophagus stimulates vagal tone priming airways for bronchoconstriction d) micro aspiration can cause bronchospasm and possibly increase inflammation in airways. e) Steroids and Theophylline can aggravate GERD due to gastric irritation and increasing acidity in stomach.

Treatment of symptomatic GERD improves control of asthma. Treatment of asymptomatic GERD is not shown to have any effect on control of asthma [20]. Our study also showed that GERD was more common in obese patients as compared to normal weight patients.

Conclusions:

1. Severe asthma is more common in overweight and obese patients as compared to patients with normal BMI and is more common in females as compared to males.

2. Obesity is associated with higher incidence of GERD and Patients with GERD have higher incidence of severe asthma.

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