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ORIGINAL RESEARCH

To Study the Link Between Metabolic Syndrome and Bronchial Asthma

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ABSTRACT

Abstract: Bronchial Asthma and Metabolic Syndrome are major public health problems that have increased worldwide. Asthma is a chronic inflammatory disorder characterized by reversible air flow limitation and hyper responsiveness of airway site n A compasses multiple phenotypes. Metabolic syndrome is comprised of hypertension, dyslipidemia obesity and insulin resistance leading to type two Diabetes Mellitus. Bronchial Asthma is a major cause of morbidity across the globe, there are several guidelines for the management of asthma including GINA, BTS but several factors still need to be addressed and asthma continues to be a major public health problem. The underlying mechanisms of interaction between bronchial asthma and metabolic syndrome need further research so as to reduce global asthma burden and to reduce its exacerbations. MS is a condition of systemic inflammation that could partially have an influence on asthma on set severity as well as its control. **Materials and Methods:** This Cross sectional study enrolled 350 patients of BA on the basis of their clinical diagnosis, supported by spirometry, blood pressure serum lipid profile, fasting and post parandial blood sugar level for diagnosing metabolic syndrome. This was analyzed to find correlation, characteristics and the determinants of Metabolic Syndrome were identified significant association was determined using latest version of SPSS statistical analysis, student t test and other relevant stats. **Results:** Our Study showed significant correlation between BA and MS as shown by p value and highlighted the importance of screening asthmatics for Metabolic syndrome and to include this in routine workup plan.

INTRODUCTION

Asthma is a multifactorial disease affecting all age groups .It is a serious global issue[1.] According to the Global Initiative for Asthma (GINA) definition, asthma is a heterogeneous disease usually characterized by chronic airway inflammation defined by a history of wheeze and dyspnoea, chest tightness and cough that vary over time and expiratory airflow limitation[2]. Various risk factors like allergens, extreme emotional responses and physical exercise, premature birth, smoking, and metabolic syndrome predispose a patient to develop asthma[3] . While the exact mechanisms underlying the association between asthma and metabolic syndrome are yet to be determined, there are significant studies to highlight bidirectional interaction between the two entities[4]. Metabolic syndrome is a condition of systemic inflammation that could partially have an influence on asthma onset and severity. According to the new IDF (International Diabetes Federation) definition, for a person to be defined as having metabolic syndrome they must have[5]

Central Obesity (defined as waist circumference for Male >90cm and Female >80cm)

Plus any two of the following four factors;

- Raised Triglycerides:>150 mg/dl (1.7mmol/L)or specific treatment for this lipid abnormality
- Reduced HDL cholesterol: <40mg/dl (1.03mmol/L) in males
- <50 mg/dl (1.29 mmol/L) in females or specific treatment for this lipid abnormality
- Raised blood pressure: systolic BP≥130 or diastolic BP≥85mm Hg or treatment of previously diagnosed hypertension
- Raised Fasting plasmaglucose: (FPG)≥100mg/dl (5.6mmol/L or previously diagnosed type2 diabetes.

Metabolic syndrome seems to contribute to longer duration as well as poor control of symptoms in asthmatics[6]. This is a rather unexplored area that could potentially open new scenarios in the diagnostic

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algorithm of the disease along with enabling a strategic approach with a more comprehensive assessment[7]. Possible correlation of metabolic syndrome affects the lung is relatively new and various studies are being conducted to establish whether there is any association between the two entities There is an increasing epidemiological link between metabolic syndrome and asthma as documented from research which needs to be further explored so as to aim for optimum disease control.

AIMS AND OBJECTIVES

- To describe the Link between metabolic syndrome and asthma in adults (15-50 years)
- To find occurrence of Metabolic Syndrome in Asthmatics, in context of their body weight, age gender etc.
- To provide data and evidence that will be useful to design strategies for optimum disease control in future.

METHODOLOGY

We used a specially designed questionnaire to obtain relevant information such as age, gender, ethnicity, asthma symptoms (shortness of breath, cough, chest tightness, allergy history, variation in symptoms), duration of asthma, and control of asthma symptoms, medication history, and family history of similar complaints. Respiratory examination was done to rule out upper airway obstruction and to look for presence of wheeze and decrease air entry. Parameters like waist circumference (cm), weight (Kg), and height (m) were then measured. Blood pressure was measured. And Pulmonary function tests were done in the sitting position using the spirometer model SPIROLAB to measure FEV_1, FVC, PEFR and post bronchodilator responses following inhalation of 200mcg salbutamol were measured.

Following investigations were done using venous blood samples in all the patients:

a) Fasting blood sugar
b) Post prandial blood sugar
c) HbA1c
d) Lipid profile (serum HDL cholesterol, serum LDL cholesterol and serum Triglyceride)
e) Serum Thyroid stimulating hormone
f) Serum vitamin D

Asthma is defined by the history of respiratory symptoms such as, wheeze, shortness of breath, chest tightness and cough that vary over time and intensity, together with variable expiratory airflow limitation.

a) FEV1 increases by >200 ml and >12% of the baseline value after inhaling salbutamol whenFEV1islow.TheFEV1/FVC is normally more than 0.75-0.80 in adults.
b) Average daily diurnal PEF variability is>10%
c) FEV1 increases by more than 12% and 200ml from baseline after 4 weeks of anti-inflammatory treatment.

2. Metabolic syndrome: It is defined as a syndrome that involves that includes following characteristics: Dyslipidemia (high levels of Apo lipoproteins and triglycerides, and/or low HDL-c), an impaired fasting glucose metabolism, hypertension or central obesity. Metabolic syndrome was diagnosed in this study according to the International **Diabetes Federation** criteria which include: Central obesity (defined as waist circumference with ethnicity specific values).

3. Asthma control was defined according to GINA guidelines. Asthma is said to be well controlled if there are none or less than twice a week daytime symptoms, no limitation of activities no nocturnal symptoms or awakening none or less than twice a week need for reliever/rescue medication in the past 4 weeks. The asthma is said to be partly controlled if any of the following is present: more than twice per week daytime symptoms, any limitation of activity nocturnal awakening, need of more than twice a week rescue or reliever treatment. Asthma is said to be uncontrolled if three or more of the partly controlled asthma symptoms are present in the last four weeks.
4. Asthma severity was assessed retrospectively from the level of treatment required to control symptoms and exacerbations. Accordingly it was classified into mild asthma (well controlled with step1or step 2 treatment. i.e. with as-needed reliever medication alone or with low-intensity controller treatment such as low dose ICS, Leukotriene receptor antagonist) moderate asthma (well controlled with step 3 treatment e.g. low dose ICS/LABA) and severe asthma (require step 4 or 5 treatment e.g. high dose ICS/LABA, to prevent it from becoming uncontrolled, or remain uncontrolled despite this treatment).
5. Cadre of BMI was classified according to **WHO criteria** in this study: underweight ($<18.5 kg/m^2$), normal ($18.5- 24.9 kg/m^2$), overweight ($25.0-29.9 kg/m^2$) and obese ($\geq 30 kg/m^2$).
6. Normal range of serum TSH is taken as 0.4to4.0mIU/L.
7. Normal range of vitamin D is taken as 30to100 ng/ml.

Statistical Analysis

Data analysis was done using JASP 0.11.1 version Statistics was applied and quantitative variables expressed as means ± SD. The Qualitative data were expressed in percentage. Comparison of means was made by student 't' test. Categorical variables were compared with the chi square test .Linear regression analysis was used for accurate data analysis..

Inclusion Criteria

- Adults with diagnosis of bronchial asthma.
- Patients who give voluntary informed consent for the study and are willing to comply with the study protocol.

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Exclusion Criteria

- Patients whose diagnosis is not yet confirmed to be Bronchial Asthma.
- Patients unwilling to participate in study.

Sample size: All the patients who visited OPD during the study period (October 2017-2019) and fulfilled the inclusion criteria are included in study.

Sampling Procedure: Participants were recruited using a convenient sampling method among adult asthmatics waiting for Check-up in the O.P.D of the hospital.

Data collection: Asthmatics attending O.P.D were recruited in the study by explaining objectives and obtaining written informed consent. Data was collected in a confidential manner using Universal techniques and precautions. The methods to measure the factors required for the diagnosis of metabolic syndrome are as follows;

After obtaining informed consent from the patient anthropometric measurements will be obtained while the participants are in light clothing.

Note: The clinical examination (BP and Waist circumference) is done on every patient as a part of regular checkup. The investigations (Lipid profile and FPGT) are also performed as routine tests for screening purposes, and no extra samples will be withdrawn for the study

1. Waist Circumference: The WHO and IDF suggest measuring waist circumference in the horizontal plane midway between the lowest ribs and the iliac crest. It is measured to the nearest 0.1 cm at the end of a normal expiration [9].
2. Blood Pressure: Blood pressure to be measured three times with a mercury sphygmomanometer while the participants are seated after 5 minutes of rest, and the three measurements average is used 10.

Data Interpretation: Data was collected and tabulated in MS-Excel. Statistical analysis of the data and correlation done by appropriate statistical tests using the latest version of the Software Statistical Package.

Ethical Considerations: The Study was approved by Institution Ethics committee.

OBSERVATIONS AND RESULTS

A total of 350 bronchial asthma patients were enrolled in the study after taking informed consent. Diagnosis of asthma was made according to the GINA guidelines. Out of 350 patients, 124 were males (35.4%) and 226 were females (64.6%).

Table 1: Gender distribution of study population

Sex	Number of patients	Percentage
Males	124	35.4%
Females	226	64.6%
Total	350	100.0%

The age range was between15and65years with a mean age of 32.3±12.3 years. There was not much gender difference in the mean age of the participants: males were33.3±12.4years and females were 31.7±12.3years (p=0.25).

Table 2: Age distribution of study population

Age groups (years)	Number of patients	Percentage
15-19	46	13.2%
20-29	140	40.0%
30-39	72	20.6%
40-49	47	13.4%
50-59	34	9.7%
60-70	11	3.1%
Total	350	100%

The mean duration of asthma was4±7.9years with the shortest duration of 2 years and longest duration of 38years.The females had significantly longer duration of asthma than the males with mean duration of 11.6±8.4 years compared with 8.2±6.5 years($p<0.05$).

Table 3: Duration of Asthma in Patients

Duration of asthma (years)	Number of patients	percentage
0-9	208	59.4%
10-19	81	23.2%
20-29	51	14.6%
30-40	10	2.8%
Total	350	100%

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The mean systolic blood pressure of the study population was 127.44±17.4 mmHg and diastolic blood pressure was 77.23±8.1 mmHg. Likewise, the mean fasting blood sugar was 98.84±21.7 mg/dl; mean serum triglyceride was 126.13±20.5 mg/dl and mean serum HDL cholesterol was found to be 51.77±10.2 mg/dl.

Table 4: Distribution of patients according to BMI (WHO criteria)

BMI of Patients (kg/m^2)	Number of Patients
<18.5	18
18.5–24.9	0131
25–29.9	68
≥30.0	133

Out of 350 bronchial asthma patients, 133 (38%) patients were obese according to WHO criteria.

Table 5: Distribution of patients according to BMI(Asia-pacific guidelines)

BMI Of Patients (kg/m^2)	Number Of Patients
<18.5	18
18.5– 22.9	100
23– 24.9	32
≥25	200

According to **Asia-pacific guidelines**, out of 350 study population, 200(57.1%) were obese**.** The mean waist circumference of the study population was 64.99±33.22 cm. The mean waist circumference of females was 68.50±34.18 cm which was significantly more than that of males with mean waist circumference58.60±30.48 cm ($p< 0.05$). Presence of obesity among asthmatics in this study was statistically significant ($p< 0.05$).

Among various components of metabolic syndrome, obesity was present in 38% of the study population followed by hypertension which was present in 28.6% of the bronchial asthma population.

24.6% of study population showed raised fasting blood sugar, 22.6% had raised serum triglyceride and 25.1% had lowered serum HDL cholesterol.

Metabolic syndrome and Bronchial Asthma: Metabolic syndrome was present in 82 patients (23%), consisting of 54 females (65.85%) and 28 males (34.15%). Presence of metabolic syndrome among asthmatics was significant ($p< 0.05$).

Table 6: Gender distribution in metabolic syndrome patients

Sex	No .of patients	Percentage
Male	28	34.15%
Female	54	65.85%
Total	82	100%

The mean age of bronchial asthma patients with metabolic syndrome was 40.40±10.9years. The mean age for females was 39.50±11.53 years and that of males was 42.14±9.63years. There was not much difference in the mean age of two groups.

Table 7: Age distribution of metabolic syndrome patients

Age groups(years)	Number of patients	Percentage
10-29	18	21.9%
30-49	46	56.2%
50-70	18	21.9%
Total	82	100%

Patients with metabolic syndrome have a longer duration of asthma symptoms as compared to those without metabolic syndrome. The mean duration of asthma was 20.72±6.51years with the shortest duration of 15 years and the longest duration of 38years.Females had a longer duration of asthma (21.87±6.91years) as compared to males (18.50±5.09years) which was statistically significant ($p<0.05$).

All patients of metabolic syndrome were obese with BMI more than 30 kg/m^2. Out of 82 patients, 53 patients belong to class 1 obesity (30-34.9 kg/m^2) of which 35 were females. 24 patients belong to class II obesity (35-39.9 kg/m^2) and 5 patients belong to class III obesity with BMI ≥ 40kg/m^2.

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Table 8: Distribution of metabolic syndrome patients according to BMI

BMI(kg/m^2)	Number of patients	Percentage
30-34.9	53	64.6%
35-39.9	24	29.3%
≥40	5	6.1%
Total	82	100%

The mean waist circumference of metabolic syndrome patients was 102.29±9.07 cm. There was no significant difference in the mean of waist circumference of females (103.51±9.39cm) and males(99.9±8.05cm),(p= 0.08) The mean systolic blood pressure of patients with metabolic syndrome was 145.71±22.17 mm/Hg and mean diastolic blood pressure was 84.71±8.48 mm/Hg. Similarly mean fasting blood sugar was 130.24±22.7mg/dl, mean serum triglyceride was155.16±10.53 mg/dl and mean serum HDL cholesterol was 36.82±7.81 mg/dl. Significant difference was present in metabolic profile of bronchial asthma patients with metabolic syndrome ($p<0.05$).

DISCUSSION

Study determines that having asthma is significantly associated with metabolic syndrome. The study estimated the prevalence of self-reported asthma as 1.8% among males and 1.9% among females. It was found that femaleswere1.2times more likely to have asthma than males (11). In present study there was no significant gender difference found in the mean age of the patients with metabolic syndrome and those without metabolic syndrome. Out of 350 asthma patients, 133 patients were obese according to WHO guidelines with BMI ≥30kg/m^2,which was quite significant. The mean waist circumference of the study population was 64.99±33.22 cm. The mean waist circumference of females was 68.50±34.18 cm which was significantly more than that of males with mean waist circumference 58.60±30.48 cm ($p< 0.05$). The presence of obesity and bronchial asthma had been epidemiologically linked in many studies.

In India and other Asian countries, central obesity is more likely to define the health risks associated with being overweight than the BMI. Asian population are however, known to be at increased risk for diabetes and hypertension at lower BMI ranges than those for non-Asian groups because of predominance of central fat distribution. This has been suggested by WHO to consider lower cut off points for therapeutic intervention in Asians populations[12].The association of the metabolic syndrome which is a cluster of conditions such as obesity hypertension, raised fasting blood sugar and dyslipidemia, with bronchial asthma is relatively a new domain. Of 350 study participants, 82 patients (23%) with bronchial asthma fulfilled the criteria required for metabolic syndrome, comprising of 54 females (65.85%) and 28 males (34.15%). Presence of metabolic syndrome among asthmatics was found to be statistically significant($p<0.05$) in this study. Similar correlation has been found in various other studies as well as documented in one of the studies conducted in Nigeria, a cross-sectional study was carried out with 158 asthmatics[13].Itwasfound that females had a longer duration of asthma with a mean duration of 16.1±13.4 years as compared with 10.7±9.2 years in males[14]. The longer duration of symptoms in females may be attributed to increased incidence of central obesity in females. Patients with metabolic syndrome had a poor control of their asthma symptoms, which was reflected by the dependency of the majority of patients on high dose ICS. Long acting β2agonist and inhaled corticosteroid were the main treatment modality among bronchial asthma patients diagnosed with metabolic syndrome in this study which shows obesity itself is a major underlying cause for poor control of symptoms. Metabolic syndrome seems to contribute to poor control of symptoms in Asthmatics. Hypothyroidism is found to be associated with decreased metabolic rate, decreased thermogenesis has been shown to correlate with a higher body mass index and a higher prevalence of obesity[16]. There has been clinical evidence suggesting that even mild derangement in thyroid function as seen in sub-clinical hypothyroidism is linked to significant change in body weight and is a potential risk factor for obesity. High levels of hormone leptin present in obese individuals has been shown to stimulate central transcription of pro hypothyroid-releasing hormone (TRH)and also that ofTRHandTSH[17].The presence of obesity and hypothyroidism was more among those patients who had longer duration of symptoms and also poor control of asthma[18]. In the present study significant correlation of metabolic syndrome with bronchial asthma was found in terms of gender ,duration of asthma and steroid dependency($p<0.05$). But there was no significant difference found in terms of age of the patients. There is underlying systemic and airway inflammation as well as oxidative stress in both asthma and metabolic syndrome.

Limitations of the study

This was a small hospital-based study, so the result of the study cannot be applied to the general population. All the participants of this study were followed for a very short span of 1-2 years. Those participants who were below the age of 20 years and were not obese needed to be followed for a longer duration so that a better association of metabolic syndrome in bronchial asthma can be elicited.

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CONCLUSION

This study aimed to find an association of metabolic syndrome with bronchial asthma, this study concluded that metabolic syndrome was significantly associated with bronchial asthma. This association is multi factorial rather than a direct linkage. Therefore every asthmatic needs to be screened for underlying metabolic syndrome especially those who are obese or hypertensive or have longer duration of asthma or poor symptoms control.

Asthmatics suffering from metabolic syndrome should not be treated for asthma alone. This is important to avoid poor therapeutic outcomes as well as to achieve optimal disease control and improve overall quality of life in patients. This approach will help in developing comprehensive strategies and treatment modalities for prevention and treatment of comorbidites in bronchial asthma.

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