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A Study of Clinical Profiles of Asthma Patients who Develop Cor-Pulmonale

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ABSTRACT

To assess the clinical profiles of patients with persistent severe asthma and evaluate them for the presence of pulmonary hypertension and Cor-Pulmonale. 30 consecutive patients with severe persistent asthma which fitted in the criteria were selected. A detailed history was obtained from them and symptom analysis was done. A detailed clinical examination was also done. Presence of pulmonary artery dilatation and other features suggestive of cor pulmonale were also looked for. The clinical profile along with the probable etiology, radiological and electro cardiographic findings were summarized and compared with existing data. Data entry was done in Epidata version 3.1 and analysis will be done using SPSS version 23.0. Minimum age was 40 years and maximum was 80 years, average age was 59.36 years. Female (86.7%) cases were more compared to males (13.3%). Majority of study subjects asthma duration was >20 years i.e. 56.6% and 10-20 years was 43.4%. Among 30 cases 63.3% (19) was found with mild Pulmonary HTN, 26.7% (8) was moderate Pulmonary HTN and severe Pulmonary HTN was found in 10%. The incidence of Cor Pulmonale was 30%. Patients with severe asthma with duration of 10 years can develop pulmonary arterial hypertension, which is the fore runner for Cor-pulmonale. Every persistent severe asthma patient with duration of 10 years of asthma should be evaluated for pulmonary arterial hypertension and Cor Pulmonale.

INTRODUCTION

Cor pulmonale is a common type of heart disease, as a result of its close association with COPD which has emerged, in recent years, as a leading cause of disability and death[1].

The diseases causing cor-pulmonale comprises those in which the impediment to pulmonary blood flow is secondary to diseases of lung and those in which the pulmonary vasculature is primarily involved[2,3].

Although the incidence is not precisely known, it is seen more frequently in patients with hypoxemia, CO2 retention and severely reduced FEV1[4].

Unlike chronic obstructive pulmonary diseases, asthma is not progressive. Although there are reports of patients with asthma developing irreversible changes in lung function, these individuals frequently have co-morbid stimuli such as cigarette smoking that could account for these findings.

Even when untreated, asthmatics do not continuously move from mild to severe disease with time. Rather, their clinical course is characterized by exacerbations and remissions[2]. So there is a controversy regarding true occurrence of cor pulmonale in bronchial asthma.

A number of asthmatic patients, usually of late onset type develop fixed airways obstruction with relatively little improvement after bronchodilators[5], but cor pulmonale in any asthmatic is rare[6]. The long history of asthma and attacks of wheezing together with eosinophilia, positive skin tests, negative Aspergillus precipitins, normal sweat test and spontaneous variation in the severity of air flow obstruction together with the absence of any smoking history or alphaantitrypsin deficiency suggests that this patient is an 'extrinsic asthmatic'. However, since many similarly affected patients do not develop CO_2 retention despite equivalent degrees of airways resistance an additional factor appears to be present in this case.

Serial measurement of the CO_2 response in patients recovering from acute asthma have shown a progressive increase in CO_2 sensitivity in all patients except those who had CO_2 retention initially[7].

Autonomic dysregulation with increased cardiac vagal activity occurs in bronchial asthma leading to enhanced neural drive to the sino-artrial node. The recurrent exposure to hypoxemia in recurrent asthmatic attacks may be one of the mechanisms which leads to substantial pulmonary vasoconstriction and narrowing of the pulmonary vasculature. Cor-pulmonale is known to occur with severe COPD. However, very little is known about the impact of persistent long standing asthma on right ventricular structure and function.

Accordingly, the present study addresses this important gap in our knowledge.

MATERIAL AND METHODS

The present study was conducted in Department of Pulmonology, Owaisi Group of Hospitals, Hyderabad

Study Site: The present study was conducted in Department of Pulmonology, Owaisi Group of Hospitals, Hyderabad.

Study Population: Patients admitted in Owaisi Group of Hospitals in the Department of Pulmonology.

Study Design: A hospital based perspective, observational study.

Sample Size with Justification: 30 patients.

Time Frame to Address the Study: From September 2016 to September 2018.

Inclusion Criteria:

- Patients reporting to the OP/IP of Respiratory Medicine Department of Owaisi Hospital and Princess Esra Hospital during the time period January 2017 – August 2018 with Persistent severe asthma
- Minimum 10 year history of Asthma
- A history of intermittent wheeze, past or current, with or without features of atopy such as allergic rhinitis, cough with exposure to household dust etc.

Exclusion Criteria:

- Smokers
- Patients historically Asthmatic for less than 10 years
- LV dysfunction
- A clinical suspicion of PTE (based on the Wells score criteria and simplified Geneva score)
- CTEPH (Chronic Thrombo Embolic Pulmonary Hypertension)
- A probable diagnosis of Sleep Apnea (by the Stop Bang questionnaire as a screening tool for OSA induced Hypertension)
- Any other condition known to cause pulmonary artery hypertension
- Calcium channel blocker or PDE-IV usage
- Pre-existing lung disorders like Bronchiectasis, Interstitial lung disease, COPD, Tuberculosis, Sarcoidosis and Occupational lung diseases

Sample Selection: Thirty consecutive patients with severe persistent asthma were selected randomly. Written informed and valid consents were taken from

the patients after providing adequate information and answering their question and queries in detail. The diagnosis of chronic cor pulmonale was made on the basis of history, physical findings and echocardiographic features.

Methodology: Thirty consecutive patients with severe persistent asthma which fitted in the criteria were selected. A detailed history was obtained from them and symptom analysis was done. A detailed clinical examination was also done. A 12 lead electrocardiogram which included right sided chest leads V3 R and V4 R was obtained and analysed. A chest radiograph which comprised of a posteroanterior chest film was obtained. In selected cases computerised tomogram of the chest was done. Parenchymal lesions in the lung were looked for which would give a clue to the underlying lung disease which caused chronic cor pulmonale. Presence of pulmonary artery dilatation and other features suggestive of cor pulmonale were also looked for.

The clinical profile along with the probable etiology, radiological and electrocardiographic findings were summarised and compared with existing data.

Investigation

- Spirometry with pre and post bronchodilator measurements
- Chest radiographs
- Blood gas analysis
- ECG
- Echocardiography

Statistical Analysis: Data entry was done in Epidata version 3.1 and analysis will be done using SPSS version 23.0.

Descriptive statistics was reported using Mean±SD for continuous variables like (age, FVC, 6-minute walk distances etc.) which are normally distributed. Categorical variables such as sex, adverse events, were reported using frequency and percentage association between the outcomes. Statistical analysis was done using chi-square test and p-value less than 0.05 was considered significant.

RESULTS AND DISCUSSION

The term 'cor-pulmonale' was introduced about 60 years ago by Paul White[8-10]. But generally little was known about this condition. In early '60s a WHO Expert Committee report focused new understanding in this sphere'[11]. The committee preferred a definition based upon morbid anatomy as this provides the only characteristic common to all patients at all stages of the disease (Table 1).

They defined it as: 'Hypertrophy of the right ventricle resulting from diseases affecting the function and/or the structure of the lung, except when these pulmonary alterations are the result of the disease that primarily affect the left side of the heart or of congenital heart disease.' Recognition of cor pulmonale rests upon demonstration of right ventricular hypertrophy[10] in the presence of the underlying causative disease. In some of these diverse clinical conditions, the abnormal signs indicative of right ventricular hypertrophy may be readily apparent in life. In other conditions, RVH may be unrecognizable. There are no symptoms specifically related to the presence of RVH. The cardiac signs are often concealed by distention of the overlying lung but may include a systolic thrust or left parasternal heave. There may be a loud pulmonary second sound. Other physical signs are either related to the severity of the pulmonary hypertension or to right heart failure (Table 2 and 3).

Though no exact data is available in Bangladesh but a hospital based study suggests more than 10% of admitted patients with heart diseases were suffering from cor-pulmonale[12]. Majumder *et al.*[13] reported that in a series of 500 cardiac patients referred for echocardiography 4.4% had cor-pulmonale. Prospective study carried out among the admitted cases of cor-pulmonale in DMCH in 1994 revealed that out of 30 cases, chronic obstructive pulmonary disease (63.33%) was the principal cause of corpulmonale. Bronchiectasis (30%) and childhood bronchial asthma (6.67%) constituted the rest (Table 4)[14].

Numerous factors may contribute to the development of cor pulmonale in patients with COPD, but its primary cause is chronic alveolar hypoxia resulting in pulmonary vasoconstriction, vascular remodelling and pulmonary hypertension[4,9,15]. The same mechanism is likely to cause development of cor pulmonale in bronchial asthma particularly in chronic or persistent variety. Although there are reports of patients with asthma developing irreversible changes

Table 1: Distribution of Study Subjects According to Age

Age	Frequency	Percent
40-50	7	23.3
51-60	8	26.7
61-70	9	30.0
>70	6	20.0
Total	30	100.0

Table 2: DISTribution of Study Subjects According to Sex

Sex	Frequency	Percent
MALE	4	13.3
FEMALE	26	86.7
Total	30	100.0

Table 3: Distribution of Study Subjects According to Duration-Asthma

Duration (Years)-Asthma	Frequency	Percent
10-20	13	43.3
21-30	7	23.3
31-40	7	23.3
41-50	3	10.0
Total	30	100.0

Table 4: Incidence of Pulmonary Htn

PULMONARY HTN	Frequency	Percent
Mild	19	63.3
Moderate	8	26.7
Severe	3	10.0
Total	30	100.0

Table 5: Association of Spirometry Report among P. Htn Groups

	Mild N = 19	Moderate N = 8	Severe N = 3	ANOVA p-value
	Mean±SD			
FVC (Pre)	2.55±0.280	2.46±0.313	2.63±0.488	>0.05
FVC (Post)	1.06±0.356	0.73±0.310	1.23±0.916	>0.05
FEV1 (Pre)	1.97±0.270	1.88±0.155	2.09±0.469	>0.05
FEV1 (Post)	0.95±0.432	0.58±0.206	0.92±0.469	>0.05
FEV1/FVC (Pre)	77.29±4.128	76.91±4.824	79.17±7.625	>0.05
FEV1/FVC (Post)	82.92±11.337	82.72±14.732	84.99±22.082	>0.05
FEF 25-75 (Pre)	2.22±0.496	2.20±0.296	2.43±0.598	>0.05
FEF 25-75 (Post)	1.09±0.873	0.617±0.250	1.34±1.192	>0.05
FEF – 25 (Pre)	5.42±0.632	5.54±1.101	5.67±1.317	>0.05
FEF – 25 (Post)	2.26±1.320	1.38±0.630	2.71±1.726	>0.05
FEF – 50 (Pre)	3.69±0.761	3.69±0.932	3.57±0.972	>0.05
FEF – 50 (Post)	3.62±10.304	0.71±0.302	1.55±1.403	>0.05
FEF – 75 (Pre)	1.42±0.538	1.33±0.484	1.23±0.418	>0.05
FEF – 75 (Post)	0.57±0.652	0.30±0.130	0.63±0.586	>0.05
PEFR (Pre)	5.83±0.740	5.91±1.142	5.97±1.336	>0.05
PEFR (Post)	2.52±1.191	1.83±0.913	3.11±1.617	>0.05

Table 6: Distribution of Study Subjects According to Cor Pul

Cor pul	Frequency	Percent
Present	9	30.0
Absent	21	70.0
Total	30	100.0

in lung function, these individuals frequently have comorbid stimuli such as cigarette smoking that could account for these findings. Even when untreated, asthmatics do not continuously move from mild to severe disease with time. Rather, their clinical course is characterized by exacerbation and remissions. So there is a controversy regarding true occurrence of cor pulmonale in bronchial asthma.

This study was performed to assess the clinical profiles of patients with Asthma who also have pulmonary hypertension, which was conducted among 30 patients of cor pulmonale at tertiary care hospital, Hyderabad.

Obviously, there is a gross underestimation of the prevalence of cor-pulmonale because routine physical examination and laboratory tests are relatively insensitive to the presence of pulmonary hypertension. The diagnostic criteria for chronic cor-pulmonale other than clinical presentation, electrocardiography and pulmonary function tests should include echocardiography. Echocardiography is believed to be a sensitive diagnostic procedure to demonstrate signs of chronic right ventricular pressure overload. But this procedure was not performed in most of the studies.

Our study has demonstrated that bronchial asthma is one of the most important underlying causes of chronic cor-pulmonale. The diagnosis of asthma was based on strong clinical history of paroxysms of shortness of breath and wheezing and adequate response to steroid treatment. These patients belong to the category of chronic persistent asthma. Bronchial asthma was presumed to be the cause of chronic cor-pulmonale in three of patients (8.8%) in Zaria, Nigeria[16]; one of 16 patients (6%) in Mombassa, Kenya[17]; 27% of 41 patients in Conakry, Guinea[18] and in none of the 134 patients in Tanzania and the 32 patients in Ethiopia[17,19].

We believe asthma as a cause of chronic cor-pulmonale has been underestimated in the past partly because of the problem inherent in its definition and the difficulty in distinguishing it from chronic bronchitis. In developing countries, many asthmatics with predominant cough, also called asthmatic bronchitis or cough-variant asthma, are often times categorized as cases of chronic bronchitis even when there is no antecedent history of cigarette smoking or exposure to industrial dusts, chemicals or fumes.

Age, Gender and Co-morbidities of Study Subjects: In present study 50% subjects were belong to above 60 years. Minimum age was 40 years and maximum was 80 years, average age was 59.36 years. This shows cases were severely affected with asthma.

Female (86.7%) cases were more compared to males (13.3%), this might be due to smokers exclusion in the study.

In present study subjects major co-morbidity was sinusitis and PND (60%) followed by GERD (53.3%) and HTN (53.3%). Others were DM in 36.7% and allergic dermatatis in 26.7% (Table 5).

Duration and Clinical Features of Asthma Among Study Subjects: Majority of study subjects asthma duration was >20 years i.e. 56.6% and 10-20 years was 43.4%.

Pedal edema was in 56.7% and raised JVP in 33.3%. On ECG Poor R progression was found in 60% and P pulmonale in 30% of study subjects (Table 6).

Incidence of Pulmonary Hypertension: Among 30 cases 63.3% (19) was found with mild Pulmonary HTN, 26.7% (8) was moderate Pulmonary HTN and severe Pulmonary HTN was found in 10% (Table 4).

X-RAY findings: In chest x-ray suggestive of PAH in 33.3% (10) cases and mild inflation was found in 66.7% (20) cases.

Spirometry Results Association among Pulmonary Hypertension Group: As all the selected cases are of persistent asthma who are already on regular management with (LABA+CS), inhalers/nebulizations /rotacaps were not stopped prior to the pulmonary function test i.e. spirometry.

This could be the reason for not having significant association between severity of pulmonary hypertension with spirometry parameters.

Blood Gas Analysis Association with Pulmonary Hypertension Group: About 19 patients out of 30 cases are with mild hypertension, 8 patients with moderate pulmonary hypertension and 3 patients with severe pulmonary hypertension.

- Grading of PAH: Up to 40 : Mild
- 40-60 : Moderate
- >60 : Severe

Maximum patients are maintaining oxygen saturation at normal air, where as some patients of moderate PAH and all the 3 patients of severe PAH are on oxygen support.

CONCLUSION

Patients with severe asthma with duration of 10 years can develop pulmonary arterial hypertension, which is the fore runner for Cor-pulmonale. Female preponderance in the study. Onset of vascular damage prior to hypoxia (PAH prior to Hypoxia). Possible dyselectrolemia and hyperglycemia in even mild pulmonary hypertension patients. With this observational study we conclude that every persistent severe asthma patient with duration of 10 years of asthma should be evaluated for pulmonary arterial hypertension and Cor Pulmonale. The onset of COR PULMONALE was not necessarily a late occurrence in Asthma patients.

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