Clinical Profile of Diseases Causing Chronic Airflow Limitation in a Tertiary Care Centre in India

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Abstract

Setting: Pulmonary department of a tertiary health care centre in India.
Objectives: To study the clinical profile of diseases causing chronic airflow limitation (CAL).
Design: Standard criteria were used for the diagnosis for various diseases causing CAL. Severity of CAL was graded using forced expiratory volume in one second (FEV₁) % predicted. Pulmonary hypertension (PH) was confirmed by 2-dimensional echocardiography with colour Doppler.
Results: Two hundred sixty eight consecutive patients of CAL, age range 12-75 years, 172 men and 96 women were included in the study. Sixty three percent had asthma, 17% had chronic obstructive pulmonary disease (COPD), 6% had bronchiectasis, 13% had obliterative bronchiolitis (OB) and 1% had occupational airway disease. 98% of COPD was caused by tobacco smoking, of which 84% were bidi smokers. Ninety-two percent cases of OB were post infectious, 78% being post tuberculosis. 37% of COPD, 33% of bronchiectasis, 53% of OB and 22% of asthma had severe airflow limitation. PH was observed in 15%, 19% and 13% cases of COPD, OB and bronchiectasis, while none with asthma had PH.
Conclusion: Although, asthma was the leading cause of CAL, it caused least functional impairment. CAL due to OB was as common as COPD. Bidi smoke was an important cause of COPD, while respiratory infection was common cause for OB. ©

INTRODUCTION

Chronic airway disease with or without chronic airflow limitation (CAL) is a major cause for morbidity. Several diseases cause CAL, notably asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis and obliterative bronchiolitis (OB). The Dutch hypothesis by Orie et al had included both COPD and chronic asthma under the broad term ‘chronic non-specific lung disease’. However, history of atopy and improvement in spirometry after bronchodilators or glucocorticosteroids point towards the diagnosis of asthma. COPD is usually tobacco smoking related and is diagnosed in presence of history of smoking. In India, bidi i.e. hand rolled cigarettes sun dried tobacco rolled in a brown, tendu leaf smoking is common accounting for 40% of tobacco consumption due to widespread availability and low cost. The prevalence of bidi smoking has been found to be high in South Asian countries.⁴ Even in United States 2.4-5.0% adolescents use bidi cigarettes believing that bids are healthy alternatives to conventional cigarettes.⁵ However bids are as harmful⁶ and have as much potential to cause clinical and functional impairment of lungs as cigarettes.⁷

Bronchiectasis though uncommon in the western world, is seen frequently in developing countries. Recent studies have shown evidence of airway obstruction in cases of bronchiectasis, which may be the dominant symptom even in patients with focal disease. Obliterative bronchiolitis (OB) is associated with small airway obstruction and is a distinct cause of CAL. The uncritical use of the term COPD perhaps leads to under diagnosis of OB.⁸ We therefore performed a prospective study of CAL in adults and adolescents, to study the clinical profile of various diseases causing CAL, the importance of bidi related COPD and role of respiratory tract infection in development of OB.

MATERIAL AND METHODS

The study was approved by the institute ethics committee. Our centre is a pulmonary unit of a tertiary care public hospital, located in India that caters to populations of diverse ethnic groups haling from different parts of the country. All adult and adolescent patients newly diagnosed as CAL from outpatient department on the basis of history and examination and investigations from January 2001 to January 2002 were included in this prospective study. Spirometry was performed with Morgan transfer test with Wyvern
software integrated pulmonary function program. Asthma was diagnosed on the basis of Global Initiative for Asthma guidelines i.e. history of paroxysmal dyspnoea and spirometry showing forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) ratio less than 70% and FEV₁ less than 80% predicted with good bronchodilator reversibility i.e. an improvement in FEV₁ by 12% and 200 ml. Diagnosis of COPD was based on Global initiative for Obstructive Lung Disease guidelines i.e. cough, sputum production, or dyspnoea with history of exposure to risk factors (e.g. tobacco smoking ≥ 20 pack-years) and spirometry showing FEV₁/FVC less than 70% and FEV₁% less than 80% predicted with poor bronchodilator reversibility. Smoking history of one pack year was taken as smoking 20 cigarettes or bidis per day for one year.

Bronchiectasis was diagnosed on the of history of chronic cough with sputum; confirmed by high resolution computed tomography (HRCT) thorax, and associated CAL by spirometry showing obstructive abnormality i.e. FEV₁/FVC less than 70% and FEV₁% less than 80% predicted. Investigations like nasal mucosal brush biopsy sweat chloride test, and serum gamma globulin levels were performed to establish the etiology of bronchiectasis.

Obliterative bronchiolitis (OB) was diagnosed by Turton’s clinical criteria, i.e. a) irreversible airway obstruction b) reduced FEV₁, and c) exclusion of emphysema, asthma, bronchiectasis or any other known causes of airway obstruction. The diagnosis was confirmed by characteristic HRCT findings of mosaic attenuation worsening on expiration. In cases of OB where HRCT showed presence of bronchiectasis in addition to mosaic attenuation, diagnosis of OB was retained as associated bronchiectasis has been reported in postinfectious OB. The two differ in clinical presentation; cases of bronchiectasis have cough with purulent expectoration even during the period of non-exacerbation, whereas cases of OB present with predominantly dry cough and dyspnoea on exertion. The etiology of OB was based on the history, clinical examination and presence/absence of underlying systemic disease.

Obstructive abnormality was graded depending on FEV₁ % predicted of 60-80%, 40-60% and less than 40% into mild, moderate and severe, respectively. Two-dimensional echocardiography with continuous and pulsed wave Doppler studies was performed in cases of clinical (loud second heart sound in pulmonary area), radiographic (dilated descending pulmonary artery) or electrocardiograph evidence of pulmonary hypertension with/without hypoxemia on pulse oximetry (saturation ≤ 92%). Pulmonary hypertension was diagnosed when Tricuspid incompetence (TI) gradient measured by continuous wave Doppler derived pulmonary artery pressure calculation was greater than 30 mm of Hg. This estimation corresponds well to pressures measured by right heart catheterisation and the error limits for Doppler derived pressure calculations are only 5-9 mm/Hg. In COPD, where it is difficult to recover a TI signal of significant quality, pulsed wave Doppler can detect pulmonary hypertension in over 90% cases, although precise calculation of pulmonary artery pressure is poor.

RESULTS

268 consecutive patients of CAL with age range of 12-75 years, 172 (64%) men and 96 (36%) women were included in this prospective study. Of the 268 patients, 169 (63%) had asthma, 46 (17%) had COPD, 15 (6%) had bronchiectasis, 36 (13%) OB and 2 (1%) suffered from occupational airway disease (Fig. 1). Clinical profiles of these diseases are given in Table 1.

The age range for asthma was 12 to 75 years, with mean age of 38 years. It was more common in men (60%) than women (40%). 13 (7%) patients were smokers, all of them with smoking index of less than 10 pack year. 71 (42%) cases had mild obstruction, whereas 60 (35%) had moderate and 38 (22%) cases had severe obstruction on spirometry (Fig. 2). 2 dimensional echocardiography was performed in 6 cases with suspected pulmonary hypertension. None of them showed evidence of pulmonary hypertension.

All the cases of COPD were above 40 years of age (Fig. 3), mean age 54 years, age range 40 to 75 years and male: female ratio of 45:1 (Table 1). 45 (98%) patients of COPD were smokers, (38 smoked bidis and 7 smoked cigarettes) while only 1 patient had exposure to biomass fuel while cooking. Bidi smokers belonged to lower socioeconomic strata and they were educated up to maximum of primary education only as against cigarette smokers who belonged to higher socioeconomic class (annual income above US $ 4800) and had received a minimum of secondary education. 14 (30%) cases presented with mild airflow limitation whereas 15 (33%) cases had moderate and 17 (37%) cases had severe obstruction on spirometry. Of 22 patients of COPD where two dimensional echocardiography was performed, 7 had pulmonary hypertension.

Bronchiectasis was seen in a younger age group, age range 13 to 54 years with a mean age of 31 years. The etiologies for bronchiectasis were (i) post infections -12 patients (80%) (ii) Dyskinetic cilia syndrome – 2 patients (13%) (iii) Tracheo bronchomegaly – 1 patient (7%). Associated small airway disease was seen in 7 patients (47%). Two of the 7 patients of bronchiectasis where pulmonary hypertension was suspected showed evidence of pulmonary hypertension on 2-dimensional echocardiography and both had associated small airway disease.

OB was the third leading cause of CAL in our study (Table 1). Mean age of OB was 45 years with the age
range of 20 to 70 years. The etiologies for OB were (i) post infectious – 33 patients (92%); 28 post tuberculous, and 5 cases had severe lower respiratory tract infection in childhood, (ii) post inhalation injury – 2 patients (6%) (iii) idiopathic – 1 patient (3%). All patients had mosaic attenuation with worsening on expiratory scans on HRCT thorax, 22 patients (61%) had associated scattered areas bronchiectasis, 4 patients (11%) had Macleod’s syndrome and 2 (6%) had associated fibrosis with atelectasis. 17 (47%) cases had moderate obstruction whereas 19 (53%) cases had severe obstruction. Of 20 cases where 2-dimensional echocardiography was performed, 7 had pulmonary hypertension.

Two (1%) men with moderate airflow limitation were diagnosed to have occupational asthma secondary to cobalt exposure in diamond polishing industry.

**DISCUSSION**

In this study, leading cause of CAL was asthma, followed by COPD, and bronchiectasis. Asthma was more common in men as compared to women. Adult asthma prevalence in India is reported to be 3.5% by physician diagnosis, and 17% using a very broad definition including those with asymptomatic bronchial hyperreactivity. Male predominance has been reported in childhood and in the elderly, while female predominance has been observed in the age group of 15 to 50 years. 13 patients (7%) were smokers but there is little evidence that smokers are at any increased risk of developing asthma. Although asthma was the leading

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**Table 1: Profile of various diseases causing chronic airflow limitation**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>BA</th>
<th>COPD</th>
<th>Bronchiectasis</th>
<th>OB</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>169 (63%)</td>
<td>46 (17%)</td>
<td>15 (5%)</td>
<td>36 (13%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Age (in years, mean)</td>
<td>38</td>
<td>54</td>
<td>31</td>
<td>45</td>
<td>41</td>
</tr>
<tr>
<td>Age Range (in years)</td>
<td>12-75</td>
<td>40-75</td>
<td>13-54</td>
<td>20-70</td>
<td>34-46</td>
</tr>
<tr>
<td>Male: Female</td>
<td>101:68</td>
<td>45:1</td>
<td>3:2</td>
<td>13:23</td>
<td>2:0</td>
</tr>
<tr>
<td>Etiology</td>
<td>Bidis Smoke-38 (83%)</td>
<td>Post infections-12 (80%)</td>
<td>Dyskinetic cilia syndrome - 2 (13%)</td>
<td>Tracheo bronchomegaly-1 (7%)</td>
<td>Cobalt exposure- (100%)</td>
</tr>
<tr>
<td></td>
<td>Cigarettes Smoke-7 (15%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Biomass fuel-1 (02%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spirometry</td>
<td>Mild obstruction</td>
<td>71 (42%)</td>
<td>14 (30%)</td>
<td>3 (20%)</td>
<td>Nil</td>
</tr>
<tr>
<td></td>
<td>Moderate obstruction</td>
<td>60 (35%)</td>
<td>15 (33%)</td>
<td>7 (47%)</td>
<td>17 (47%)</td>
</tr>
<tr>
<td></td>
<td>Severe obstruction</td>
<td>38 (22%)</td>
<td>17 (37%)</td>
<td>5 (33%)</td>
<td>19 (53%)</td>
</tr>
<tr>
<td>2-D ECHO*</td>
<td>6</td>
<td>22</td>
<td>7</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>0</td>
<td>7</td>
<td>2</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>No pulmonary hypertension</td>
<td>6</td>
<td>15</td>
<td>5</td>
<td>13</td>
<td>2</td>
</tr>
</tbody>
</table>

* Number of patients with data available: COPD- Chronic obstructive pulmonary disease; OB- Obliterative bronchiolitis; BA- Bronchial asthma; 2-D ECHO- 2 Dimensional echocardiography
cause of CAL, it led to least degree of airflow limitation (Fig. 2). Pulmonary hypertension was not present in any of the cases with asthma. This is because asthma causes a reversible CAL; and is very rarely associated with pulmonary hypertension.9

COPD is a major cause of ill health and death in adults. It is reaching epidemic proportions in third world, principally as a result of increased tobacco consumption. An attempt was made earlier to estimate the gross burden of COPD and its smoking association by reviewing the population studies available from India. The median values of different prevalence rates (i.e. 5 percent in male and 2.7 percent in female population) were accepted as the most appropriate figures to calculate the overall estimates.10 In a recent large, multicentric study11 the population prevalence of COPD in India has been shown to be 4.1 per cent of 35295 subjects with a male to female ratio of 1.56:1 i.e., a prevalence of 5.0 per cent among men and 3.2 per cent in women. COPD was the second common cause of CAL after bronchial asthma in our study. All patients presented after 40 years of age and men outnumbered women (Fig. 2). COPD patients have a relatively late presentation, usually after fourth decade. Historically more men have been affected however women are rapidly catching up especially in the developed countries. In our study 83% cases of COPD were bidi smokers. Although a bidi contains about one-fourth the amount of tobacco compared to a cigarette, it delivers a comparable amount of ‘tar’ and contains higher concentrations of nicotine than cigarettes.3 The time to smoke and number of puffs are significantly greater while smoking a bidi as bidis self-extinguish.1 A bidi is thus no less dangerous than a cigarette. In our study, 83% of COPD cases were bidi smokers. We also found that bidi smoking was inversely related to socioeconomic status and education similar to a study by Chhabra et al.4 In India, it is estimated that indoor air pollution (biomass fuel) is an additional important risk factor for COPD.12 However, in the present study only one patient had COPD due to biomass fuel. Pulmonary hypertension was seen in 15% of patients of COPD. Pulmonary arterial hypertension and cor pulmonale are related to relatively blunt respiratory center responsiveness to hypoxia and hypercapnia.

Six percent of patients with airflow limitation in our study were diagnosed to have bronchiectasis. CAL in bronchiectasis is due to associated small airway disease, different pro-inflammatory mediators contributing to recruitment of neutrophils to the inflamed airways and increased incidence of bronchial hyperreactivity due to increased epithelial permeability,13 which allows access to toxins through inflamed bronchial mucosa. The severity is related to the duration of sputum production and is independent of the extent of bronchiectasis.

Patients of bronchiectasis presented at a relatively younger age, the mean age of presentation being 31 years, similar to a previous studies. Commonest etiology was lower respiratory tract infection (80%) usually in childhood, followed by hereditary disorders like dyskinetic cilia syndrome (13%) and tracheobronchomegaly (7%). Our findings were similar to a North American study where 70% cases of bronchiectasis were attributed to childhood pneumonia and the remainder to congenital anomalies.14 HRCT is indicated in cases of bronchiectasis for detecting extent and cause of disease and associated small airway abnormality.6 HRCT showed associated small airway disease in 7 patients of bronchiectasis in the present study. Functional evidence of small airway disease is reported to be common even when the bronchiectasis is mild.6 This is explained by chronic infection in the bronchiectatic airways, which spreads peripherally and thus obliterates the peripheral bronchi. Also, initial viral infection in cases of postinfectious cases may lead to simultaneous injury to bronchi and bronchiole that result in small airway obstruction, which may become established as a result of repeated bacterial infections.6 These cases with evidence of associated small airway disease on HRCT have higher incidence of pulmonary hypertension due to greater airflow limitation. Of the 15 patients of bronchiectasis, pulmonary hypertension was present in 2 cases both with associated small airway disease.

OB continues to be increasingly recognized as a cause of airflow obstruction.14 A significant finding of our study was that CAL due to OB (13%) was as common as COPD (17%). COPD and OB have a common clinical presentation. The difference is in age of presentation and progression of disease; cases of OB present earlier in life and may have a rapidly declining course leading to early pulmonary hypertension. The mean age of presentation of OB in our study was 45 years compared to 54 years in the COPD group. Pulmonary hypertension was seen in almost equal number of cases however patients of OB had more severe airflow limitation. The diagnosis of OB based on Turton’s clinical criteria was confirmed by presence of mosaic attenuation worsening on expiratory scan. HRCT showing areas of mosaic attenuation with air trapping on expiratory scan in correct clinical context is diagnostic of OB.7,15,16,17 Open lung biopsy, once considered to be the gold standard is not necessary for diagnosis of OB.16,17 HRCT features occur even before measurable evidence of airflow obstruction. Other associated findings are chronic atelectasis, bronchiectasis, and Macleod’s syndrome as noted in our study.7

Ninety-two percent cases of OB were post infectious in etiology as against countries where OB is commonly associated with lung, heart-lung and bone marrow transplant and collagen vascular diseases. Postinfectious nature of the disease was based on previous history and as the diagnosis was made long after the initial insult,
the exact etiological agent could not be identified in all cases. However, in 28 patients (78%) symptoms of CAL began following an episode of pulmonary tuberculosis. The diagnoses in these cases were obtained from the past records available with the patient. OB following lung infections with Mycobacterium avium intracellular and Mycobacterium tuberculosis has been reported in literature. In India since the prevalence of tuberculosis is high, it is likely to be an important cause of OB. Naidoo et al showed that black coal miners with a past history of tuberculosis had reductions in the FEV1, and FVC% predicted of 20% and 14%, respectively. Hnizdo et al showed that tuberculosis can cause chronic airflow impairment. In these studies obstructive abnormality on spirometry was probably due to postinfectious OB. We suggest that HRCT thorax should be performed in cases with “posttuberculous bronchitis” to rule out OB. 5 (14%) patients of OB in the present study were symptomatic since childhood and had histories of severe respiratory tract infections prior to the onset of symptoms. Post infectious OB persists for years after its onset in childhood and worsens due to exacerbations caused by viral infections, suppuration, atelectasis, and pneumonias. Kim et al observed that OB in children is not as lethal as has been reported previously. We presume that children who survive the initial insult may present later in life when the disease worsens. 53% cases had severe obstruction and 19% cases had developed pulmonary hypertension at the time of presentation. OB has been reported as an important cause for pulmonary hypertension and cor pulmonale.

Occupational CAL was seen in 2 patients exposed to cobalt dust while working in the diamond polish industries. The bronchoconstrictive reaction to cobalt dust has been attributed to specific allergic effect (in which cobalt particle acts as a hapten) rather than to a toxic irritant effect.

To conclude, the findings of our study suggest that although asthma was the leading cause of CAL, it caused least degree of functional impairment. OB was an important cause of CAL and was seen as frequently as COPD. Bidi smoke was an important etiology for COPD, while infectious disease including tuberculosis was the most common etiology for OB. Thus, detailed history of respiratory tract infection and HRCT thorax should be sought for, in cases of undiagnosed CAL.

REFERENCES