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CAUSES AND CLINICAL CHARACTERISTICS OF CHRONIC COR-PULMONALE IN ETHIOPIA
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ABSTACT

Objective: **To determine the clinical characteristics and underlying causes of chronic cor-pulmonale in Ethiopian patients.**
Design: **A hospital based cross-sectional study.**
Setting: **Tikur Anbessa Hospital, a large referral hospital in Addis Ababa, Ethiopia.**
Subjects: **Fourty two consecutive patients referred to the chest clinic of Tikur Anbessa Hospital, Addis Ababa, Ethiopia.**
Results: **Bronchial asthma (36%), chronic fibrocavitary tuberculosis (31%) and chronic bronchitis/emphysema (33%) were the most frequent underlying causes and occurred either singly or in combination in 36(86%) of patients. Interstitial lung disease occurred in five (11.9%) patients. Right-sided heart failure and cyanosis were the most common clinical presentations. Secondary polycythemia was noted in 32 of 40 patients (80%). The role of pulmonary vascular diseases including pulmonary schistosomiasis as a cause of pulmonary heart disease could not be ascertained but appeared to be insignificant.**
Conclusion: **Chronic persistent asthma is a frequent underlying cause of chronic obstructive pulmonary disease and chronic cor-pulmonale compared to smoking related chronic bronchitis/emphysema in Ethiopia. The preventive strategy of chronic cor-pulmonale includes optimal treatment of bronchial asthma, early diagnosis and effective treatment of tuberculosis and health education to avoid cigarette smoking.**

INTRODUCTION

Cor-pulmonale is far less a problem in African countries than in Europe and North America where smoking related chronic obstructive pulmonary disease (COPD) is common and more than half of these develop the disease (l). In many countries in Africa, the reported prevalence amongst cardiac patients ranges between none to 15% (2-6). In Ethiopia, cor-pulmonale comprised between 1.6% and 6.5% of all hospitalised cardiac cases in the past (7-11). The first report of 32 cases of chronic cor-pulmonale by warell *et al* (11) in 1969 had shown that chronic bronchitis and pulmonary tuberculosis constituted 75% of the underlying causes.

Several African countries have reported bronchial asthma as a possible cause of chronic cor-pulmonale (4,5,12). However, there was no mention of asthma in the Ethiopian study. To the contrary, our clinical observation at Tikur Anbessa Hospital indicates that chronic cor-pulmonale is a frequently associated disease with bronchial asthma. The present study was undertaken to re-examine the pattern of chest diseases associated with chronic cor-pulmonale in Ethiopian patients as seen at Tikur Anbessa Hospital (TAH).

MATERIALS AND METHODS

Forty two consecutive adult patients referred to the chest unit of Tikur Anbessa Hospital and diagnosed to have chronic cor-pulmonale on the basis of suggestive clinical, chest X-ray and electro-cardio graphic findings were included in the study. The diagnosis of cor-pulmonale was made whenever one or more of the following criteria were met.

Clinical: Shortness of breath with right-sided heart failure including elevated JVP, loud p2, right-sided fourth heart sound, tricuspid regurgitation and peripheral edema.

Chest X-ray: Enlargement of the central pulmonary arteries, cardiomegally and/or signs of emphysema.

Electrocardiography: Right axis deviation, p-pulmonale in lead 2 or 3, R/S amplitude greater than 1 in lead V1, and poor r wave progression. All patients had a detailed clinical examination including a history of smoking and current or past treatment for tuberculosis and an erect PA and lateral chest X-ray. Thirty nine patients had a 12 lead electrocardiogram and airflow measurement using a Spirometer (P.K. Morgan UK) and Wrights peak flow meter. Both the forced expiratory volume in one second (FEV1) and the forced vital capacity (FVC) were measured before and 10 to 15 minutes after administration of 200 micrograms of salbutamol delivered from a metered dose inhaler (MDI). A change in FEV1 by 12% or more after application of bronchodilator was considered as suggestive of reversible airway disease (asthma). Those patients who failed to respond to bronchodilator inhaler were subsequently put on tapering dose of predinsolone and rechecked two weeks later. In the absence of a background history of cigarette smoking and the presence

of a typical history of paroxysms of dyspnoea and wheezing, those who showed significant improvement were considered as having bronchial asthma. A diagnosis of an old fibro-cavitary tuberculosis was made on the findings of a fibro thorax on a chest X-ray, negative sputum smear for AFB and past treatment history for tuberculosis. Chronic bronchitis/emphysema was diagnosed in patients with non-paroxysmal dyspnoea, irreversible airflow limitation by spirometric measurement and often times a history of cigarette smoking. A diagnosis of interstitial lung disease was made from a suggestive history of progressive shortness of breath and bilateral interstitial infiltrates on a chest X-ray. We were not able to determine diffusion capacity, alveolar-arterial gradient, static lung volume and also perform echocardiography and blood gas analysis due to lack of equipments.

Haemoglobin and haematocrit were determined in 40 patients. Secondary polycythemia was diagnosed whenever the haemoglobin or haematocrit values exceeded 17gm% or 58% for males and l6gm% or 53% for females respectively. The upper limit for the normal haemoglobin and haematocrit were taken from the mean +/-2SD values of a previous study by Hofvander (13). An indirect measurement of alpha-l anti-trypsin deficiency was made from the alpha-l globulin fraction of the serum protein in 27 patients.

RESULTS

Clinical characteristics: Of the 42 patients, 55% were male and the overall median age was 50 years (range 25-77). The mean duration of illness prior to developing heart failure was 12.9 years. Cyanosis and right-sided heart failure were the most frequent clinical findings and occurred in 39(93%) and 36(86%) patients respectively. Clubbing of finger nails occurred in 19(45%) patients and all had cyanosis. Wheezing occurred in 19(45%) patients and all but two had bronchial asthma. Neurological manifestations including flapping tremor, disorientation, loss of memory and lack of abstract thinking (Global brain dysfunction) occurred in nine (21%) patients. Secondary polycythemia was noted in 32 of the 40 patients (80%). The mean (SD) haemoglobin and haematocrit was 18.6 (2.72) gm/dl and 62.1% (8.12) respectively. The alphal-globulin fraction of the serum protein was normal in all the 27 patients, suggesting that alpha-1-anti-trypsin deficiency was an unlikely cause of the emphysema. The details of the clinical presentation are shown in Table 1.

Table 1

Clinical signs and symptoms in 42 patients

Clinical characteristics	No. (%)
Age - mean (range) years	51(25-77)
Duration of illness-mean range(years)	12.9(4month-57yrs)
Childhood respiratory illness	4(9.5)
Exposure to cooking fire, chemicals	4(9.5)
Allergic rhinitis	13(31)
Cigarette smoking	12(28.5)
Cyanosis	39(93)
Clubbing	19(45)
Wheezing	19(45)
Accentuated P_2	6(14)
Right side gallop rhythm (S_3)	7(17)
Flapping tremor + GBD*	9(21)
Congestive heart failure	36(86)
2° Polychthemia	32/40(80)
EKG evidence for cor-pulmonale	33/39(85)
C-X-ray evidence for cor-pulmonale	26(/39(67%)
Spirometry (obstructive pattern)	26/39(67%)
- restrictive pattern	7/39(17)
- combined	6/39(14)

*Global Brain Dysfunction

Underlying causes: The causes and patient characteristics associated with chronic cor-pulmonale are shown in Table 2. A total of 50 diagnoses were made of which a single underlying cause was identified in 32 patients (76%). In the remaining 10 patients, a combination of two diseases were diagnosed.

Table 2

Patient characteristics and causes associated with chronic cor-pulmonale in Ethiopian patients

Underlying causes	No. of diagnoses (n=50)(%)	Median age(range) in years	No. of smokers (%)	Duration illness in Mean(SD)
Bronchial asthma	15	50(30-70)	2(13%)	23(14.12)
Pulmonary tuberculosis	13	38(25-65)	0	8.38(6.67)
Chronic bronchitis/ Emphysema	12	60(43-77)	11(92%)	21(18.04)
Interstitial lung disease	5	51(40-58)	0	3.5years
Bronchiectasis	2	46	1	7
Obesity	2	63	0	-
Kypho-scolosis	1	30	1	-

Chronic fibro-cavitary tuberculosis was diagnosed as the single most likely cause of cor-pulmonale in nine patients (21%). In two patients each, it occurred along bronchial asthma and chronic bronchitis/emphysema. In all except one patient, the chest X-rays were suggestive of old, burnt out tuberculosis with residual fibrotic changes. Six patients had unilateral fibro-thorax, five patients had bilateral extensive fibrosis with involvement of the apices of the lungs and two patients had bilateral fibrosis with cavities.

Bronchial asthma was diagnosed in 15 patients (36%) and it was the single most likely cause in nine patients (21%). In the remaining six patients, it occurred along chronic bronchitis (two patients), chronic fibro-cavitary tuberculosis (two patients) and chronic interstitial lung disease (two patients). In all the 15 patients, spirometric measurement of lung function showed moderate to severe airflow limitation. In seven patients, the obstruction was either not reversible or only mildly reversible with bronchodilator inhalers. Diagnosis of asthma was made on the basis of typical history of paroxysms of dyspnoea and wheezing, absence of a history of cigarette smoking and adequate response to oral steroid treatment. All 15 patients had either perennial or frequent intermittent attacks of asthma. The mean duration of illness was 23 years before they developed chronic cor-pulmonale. Two patients had chronic childhood respiratory illness. Two more patients gave a history of cigarette smoking 40 and 30 pack years respectively and were categorized as having both bronchial asthma and chronic bronchitis.

Chronic bronchitis/emphysema was diagnosed as the single most likely cause in eight patients (19%). In 4 more patients it occurred along bronchiectasis (one patient), extreme obesity (one patient) and chronic fibro-cavitary tuberculosis (two patients). Eleven of the 12 patients (92%) gave a history of smoking for a mean duration of 37 pack years. Three female patients admitted to cooking over an open fire in poorly ventilated huts for many years. These three patients each had bronchial asthma, tuberculosis or interstitial lung disease at the same time. One patient working in a printing press had been exposed to chemical fumes for many years. This patient had severe asthma too. Amongst the eight patients with chronic bronchitis/ emphysema alone, seven patients had moderate to severe airflow limitation. Four patients had chest X-ray finding of hyper-inflated lung with flattening of the diaphragm suggestive of emphysema.

Interstitial lung diseases were diagnosed from chest X-rays alone in five patients. Two of these patients had bronchial asthma too. An etiologic diagnosis could not be made in these five patients. Bronchiectasis and extreme obesity with Pickwickian syndrome were identified in two patients each.

DISCUSSION

The prevalence of chronic cor-pulmonale among admitted and outpatients in African countries has varied between none in two large studies from cardiology referral clinics in Addis Ababa and Nairobi (14,15) and 15% to 27% from reports from Zaria, Nigeria(4) and Conakry, Guinea(12) respectively. Chronic pulmonary heart disease was the third most common cause of congestive cardiac failure following hypertensive heart disease and congestive cardiomyopathy in elderly patients in Zaria, Nigeria(4). However, it accounted for only 3% of admissions of all age groups over a 10 year period at Ahmadu Bello University in Zaria, Nigeria(5). In developed countries, cor-pulmonale accounts for 5-15% of all organic heart diseases(l) .

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. Besides, most of the above mentioned studies were done in patients who have already developed congestive heart failure. 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 from Africa including ours. Our study has demonstrated that bronchial asthma is one of the most important underlying causes of chronic cor-pulmonale. In seven out of 15 patients, the response to bronchodilator was inadequate and 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 34 patients (8.8%) in Zaria, Nigeria (4), one of 16 patients (6%) in Mombassa, Kenya (3), 27% of 41 patients in Conakry, Guinea (12) and in none of the 134 patients in Tanzania and the 32 patients in Ethiopia (3,11). 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. In the previous Ethiopian study, 18 of the 32 patients (56%) with chronic cough and wheezes were categorised as

cases of chronic bronchitis in the absence of a history of cigarette smoking, exposure to industrial dusts and chemicals or significant history of childhood respiratory illness. It is probable that most of these patients were cases of bronchial asthma. The distinction between cough-variant asthma and chronic bronchitis/emphysema is often times difficult unless the diffusion capacity for carbon monoxide is measured. Diffusion capacity is usually normal in asthma and markedly reduced in chronic bronchitis/emphysema. In many developing countries including ours, the treatment offered to patients with bronchial asthma is often times suboptimal because of lack of drugs and/or inappropriate prescriptions. Besides, there is a gross under-use of steroids, failure to adhere to prescribed doses and lack of follow-up visits by patients. This will inevitably allow the asthmatic diathesis to run an irreversible course and lead to the development of sustained pulmonary hypertension. Bronchial asthma is even less considered as a cause of cor-pulmonale in developed countries(17-19) although autopsy studies have shown that right ventricular hypertrophy occurs in 6% to 20% of chronic asthmatics (20-22). This is probably because smoking related COPD dominates the spectrum of diseases that cause cor-pulmonale. It is also known that bronchial asthma can cause irreversible airway obstruction and the degree of obstruction is a function of the severity and duration of illness (23, 24). Besides, autopsy studies of the bronchial wall in patients who die of status asthmaticus and severe asthma have shown the presence of mucus plugs, thickening of the basement membrane and smooth muscle hypertrophy (20,25). Such findings suggest that bronchial asthma is a potential cause of chronic cor-pulmonale. In patients with a history of smoking and asthma, there will inevitably be an overlap between chronic bronchitis and asthma.

Tuberculosis occurred in relatively younger patients and the mean duration of illness was shorter compared to bronchial asthma and chronic bronchitis. Tuberculosis was reported as a cause of cor-pulmonale in 23.5% and 19% of patients from Zaria, Nigeria(4,5), 22% from Addis Ababa(12), and 12.5% from Mombassa, Kenya(16). The occurrence of chronic complication of tuberculosis in young people at a rate similar to what was reported 33 years ago in this country lends to the opinion that the diagnosis and treatment of tuberculosis is far from satisfactory.

Chronic bronchitis/emphysema occurred in older patients and 92% of these were smokers. Parry *et al*. have suggested that in Africa, women who have cooked over a fire in poorly ventilated huts are vulnerable to develop COPD and subsequently cor-pulmonale (26).The three housewives who gave a similar history in our study also had other underlying causes to account for the cor-pulmonale. As the sample size in this study was small, it will be difficult to determine the relative contribution of this practice to the development of COPD and chronic cor-pulmonale but appears to be very little.

In Egypt and several other African countries, pulmonary schistosomiasis has been identified as a cause of chronic cor-pulmonale (5,27). In autopsy material consisting of medico-legal cases in the Sudan, *S.mansoni* and *S.haematobium* infections were observed in 14.3% and 4.5% respectively. However, cor-pulmonale was rarely encountered (28). In none of our patients had schistosomiasis been considered or suspected to be the cause of pulmonary heart disease.

In developed countries, pulmonary vascular diseases such as recurrent pulmonary emboli and primary pulmonary hypertension are considered to be important causes of chronic cor-pulmonale. The diagnosis of such conditions is difficult in developing countries and their relative contribution to the prevalence of cor-pulmonale is unknown but appears to be rare.

In conclusion, our study has demonstrated that bronchial asthma followed by tuberculosis and chronic bronchitis/ emphysema are the most frequent causes of chronic cor-pulmonale. The preventive strategy should, therefore, stress on optimal treatment of bronchial asthma, early diagnosis and effective treatment of pulmonary tuberculosis and health education to prevent cigarette smoking.

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