PREVALENCE AND CAUSES OF CHRONIC DRY COUGH AT A RESPIRATORY CLINIC IN TRIPOLI A PROSPECTIVE STUDY BY

Masaud Azzabi[1], Mahdia Buargub[1], Rajab Tarsin[2], Jalal Zantuti[1], Ishrak Ishamli[2]

1- Tripoli Central Hospital
2- Tripoli Medical Center

ABSTRACT

Prolonged dry cough, in the absence of other features that suggest common etiologies, can be a diagnostic challenge. The aim of this study was to examine the prevalence and causes of isolated chronic dry cough among the patients who presented to the respiratory clinic in Tripoli Central Hospital during the period from 1st Jan 2005 to 31st Dec 2009. In this prospective study, data from the patients who met the following inclusion criteria was collected; complaint of isolated dry cough for more than 8 weeks, normal chest radiograph, chest physical examination and basal spirometric values. The post-bronchodilator improvement in the FEV1 was considered significant and suggestive of cough variant asthma if it exceeded 15% of the baseline value. The diagnosis was confirmed if the cough improved or disappeared after a short course of steroid therapy. The diagnosis of reflux associated cough was confirmed if it improved with anti-reflux therapy. The total number of registered patients was 800; 69 consecutive patients (8.6%) met the selection criteria. The mean duration of cough was (± SD) 113 ± 141 weeks (range; 8-720 weeks). Their mean age (± SD) was 32 ± 13.2 years (range; 15-75 yrs). Thirty- nine were females (56.5%), and 8 were current or ex-smokers (11.5%). In 56 patients (81.15%) the likely diagnosis was cough variant asthma (CVA). Out of them; 45 (80%) had associated allergic rhinitis too. All of the CVA patients received a short course of oral steroids in addition to bronchodilator inhalers. In another 7 patients (10.1% of total and mostly males (71.4%)); the likely diagnosis was gastro-esophageal reflux disease (GERD) related cough and they responded to anti-reflux therapy. In the last 6 patients (8.7%) who were male smokers; no clear diagnosis was established. They received bronchodilator therapy and were advised to stop smoking. CVA was highly prevalent cause of chronic cough (81.15%) in the study group. Most of the CVA patients had rhinitis too (80%) and the contribution of post nasal drip to the etiology of cough is difficult to establish. 56.5% of the CVA patients were females and of younger age. GERD related cough was less prevalent (10.1%) and was mostly in males.

KEY WORDS: Chronic dry cough, Cough variant asthma

INTRODUCTION

Chronic cough is defined as persistent cough for more than 8 weeks, and is the sole presenting complaint of 10–38 % of referrals to respiratory physicians[1-3]. It can impair the quality of life, resulting in sleep disturbance, anxiety, fatigue, myalgia, dysphonia, syncope, or urinary incontinence; it also results in a high rate of healthcare utilization[3]. Significant sputum production usually indicates a primary lung pathology .The most common causes of chronic dry cough in non-smoking, non- ACE-inhibitor treated adults with normal chest radiogram are; postnasal drip (PND), gastro -esophageal reflux disease (GERD) and asthma syndromes[5].

Asthma syndromes include; "classic" asthma, cough variant asthma (CVA), non-asthmatic eosinophilic bronchitis and atopic cough. CVA was described in 1979 by Corrao and colleagues[6] as; Air way hyper-responsiveness (AHR) with chronic cough but without wheeze or airway obstruction.

CVA is a possible precursor of classic asthma; it usually improves within 1 week of inhaled bronchodilator therapy. Inhaled corticosteroid therapy improves the cough and may reduce the risk of progression to classical asthma[7, 8].

'Atopic cough' is a bronchodilator resistant chronic dry cough, characterizes by absence of variable airflow obstruction and the presence of atopy[7, 8, 9].

Patients with asthma syndromes may present a diagnostic challenge, awareness of them and the ability to diagnose and treat them early; relieves the patient morbidity and may prevent progression into classic asthma[9]. The aim of this prospective study was to examine the causes, characteristics & outcomes of chronic cough among the registered patients at the outpatient respiratory clinic in Tripoli central hospital during the period from 1st Jan 2005 to 31st Dec 2009.

METHOD & PATIENTS

Patients who presented to the respiratory clinic with the sole complaint of chronic dry cough for more than 8 weeks were included in the study, the following

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Correspondence and reprint request :
Masaud Azzabi..
Tripoli central hospital
Email : mezzabi @yahoo.com

were the inclusion criteria; 1) No history of asthma, no therapy with ACEI therapy or beta blockers, 2) Normal chest physical examination, 3) Normal chest radiology, and 4) Baseline forced vital capacity (FVC) more than or equal to 70% of predicted values. 69 consecutive patients were included.

The collected data included; diurnal variation and exacerbating factors of the cough, personal or family history of allergic disease, smoking history, esophageal symptoms and presence of blood and sputum eosinophilia. The response of forced expiratory volume (FEV1) to short-acting beta2-agonist bronchodilator therapy was considered significant if it improved by more than 15%.

Spirometry was performed using the Quark PFT® spirometry system (COSMED) and according to the American Thoracic Society (ATS) guidelines. Spirometry was recorded before and after Ventoline inhalations doses that were repeated at intervals of a minimum of 30 minutes.

Peripheral blood eosinophilia was considered significant if it was more than > 6% of total WBC counts, and sputum eosinophil count was considered significant if was equal to or more than ≥ 3%.

Going with the European society guidelines[1]; CVA suspected patients were prescribed a two weeks course of 20 mg prednisolone and bronchodilator therapy, while GERD associated cough suspected patients were treated with a two weeks course of omeprazole 20 mg tab and bronchodilators .

Data analysis

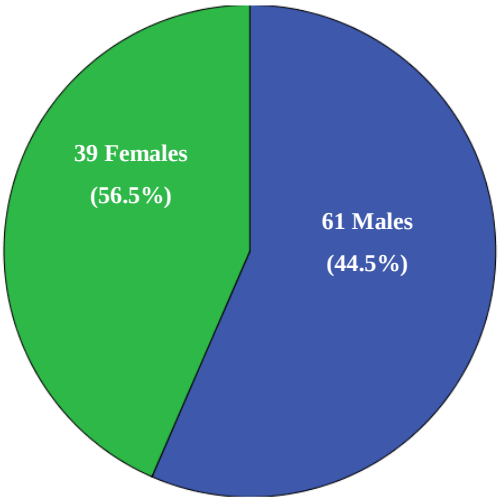
The SPSS software (Statistical Package for the Social Sciences, version 16.0 (SPSS Inc, Chicago, Ill, USA) was used for statistical analysis). Continuous variables are demonstrated as means (±SD), and categorical variables as numbers and percentages. Characteristics of the groups were compared using analysis of variance (ANOVA) for continuous variables& student's t-test for categorical variables. P less than 0.05 was considered significant.

RESULTS

During the study period; a total of 800 patients presented to the respiratory clinic and 69 of them (8.6%) met the selection criteria. As shown in (table 1); their mean age (± SD) was 32 ± 13.2 years (range; range; 15-75 yrs), 39 were females (56.5%) (figure 1), and 9 were current or ex-smokers (11.5%).

The mean duration of chronic dry cough was (± SD) 113± 141 weeks (range; 8-720 weeks). All of them had baseline FVC values more than 70 percent of predicted and FEV1 mean value of (± SD) of 72.4 ± 2.4 percent of predicted. Their mean blood eosinophil count value was 309 ±194 /cmm.

Out of the 69 patients; 56 patients (81.15%) had CVA (figure 2), methacholine inhalation challenge testing was not performed, however; the significant (> 15%) post bronchodilator improvement in FEV1 and the resolution of cough with anti-asthmatic therapy were considered diagnostic[1].

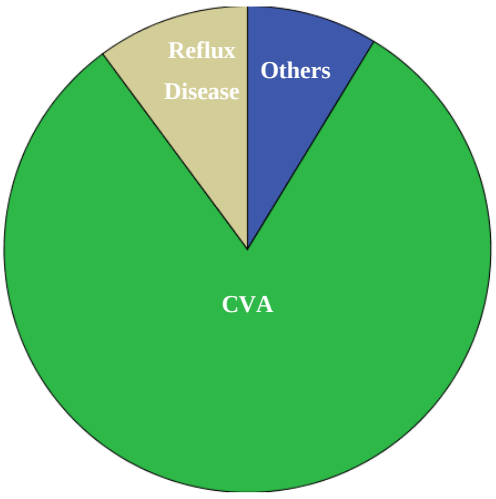


(Figure 1) Gender distribution of the studied patient

(Table 1) Demographic Characteristics of the study patients

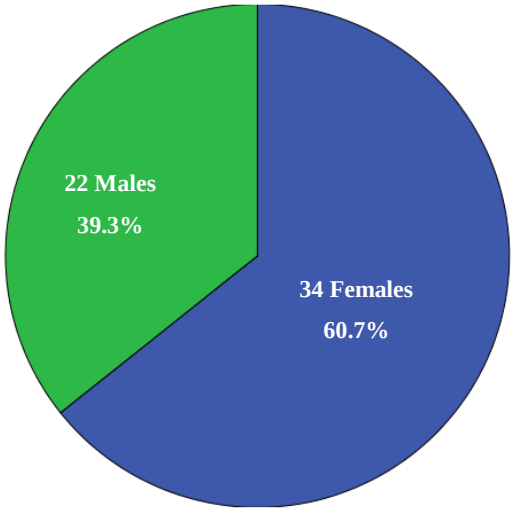
Age (yrs)	**32 ± 13.2**
Gender (female)	56.5%
Cough duration (weeks)	113 ± 141
Diurnal variation (yes)	72.4%
Seasonal variation (yes)	17.3%
Dust intolerance (yes)	68%
Allergic rhinitis (yes)	65.2%
Skin allergy (yes)	11.59%
Food allergy (yes)	5.79%
Conjunctival allergy (yes)	23%
Family history of allergy(yes)	53.6%
Smoking (yes)	13%
Blood Eosinophilia	24.6%
Sputum eosinophils (yes)	49.3%
Baseline FVC(% of predicted)	>70
Baseline FEV1 (% of predicted)	72.4 ± 2.4
Values expressed as % or mean ± SD	

As shown in (table 2); 34 of the 56 CVA patients were females (60.7%) (figure 3), all of them had dry cough, exacerbated by dust and noxious substances exposure, diurnal variations was reported by 49(87.5%) patients (the cough was more sever and frequent night and or early morning). Personal and / or family History of



(Figure 2) Causes of chronic cough

allergic diseases (rhinitis, eczema, allergic conjunctivitis, or food allergies) was reported in 32 (57.1%) and 45 patients (80%) had rhinitis. Fifteen patients had blood eosinophilia > 6% (26.7 %), with a mean value of 603/cmm. Sputum eosinophils were detected in 33 (58.9 %) patients.



(Figure 3) Gender distribution of CVA patient

The post-bronchodilator improvement in FEV1 was attained after the 1st bronchodilator test dose in 23 pts (41%), the 2nd test dose in 27 patients and the 3rd test dose in 6 patients. Seven 7 out of the 69 studied patients (10.1%) had GERD and their cough responded to reflux therapy, 5 of them were males (74.1%). The chronic cough in the other 6 patients (8.7% and all males) was probably related to smoking.

(Table 2) Diagnosis & characteristics' of the studied chronic cough patients

Cough variant Asthma	**81.15%**
Gender (F)	60.7%
Age (yrs)	30.5 ± 12
Cough duration (weeks)	121.5 ± 148.8
CVA only	10.7%
CVA + rhinitis	80%
CVA + history of allergy	57.1%
Diurnal variation (yes)	87.5%
Smoking (yes)	3/56
Blood eosinophilia (/cmm)	324 ± 148.8
Sputum eosinophils	58.9%
Baseline FEV1 (% predicted)	72.4 ± 2.55
Post bronchodilator ↑in FEV1(% predicted)	
↑FEV1≥ 15% after the 1st test dose	41%
↑FEV1≥ 15% after the 2nd test dose	48%
↑FEV1≥ 15% after the 3rd test dose	10.7%
Reflux	10.1%
Gender (Males)	71.4%
Age (yrs)	36.5 ± 7.1
Smoking (yes)	14.2%
Cough duration (weeks)	33 ± 26.7
Cigarette smoking	8.7%
Gender (Males)	100 %
Age	58.25 ± 14.2
Smoking (yes)	100%
Values expressed as % or mean ± SD	

Statistical analysis as shown in (table 3), revealed significant associations between the age of the patient with both the post bronchodilator FEV1 value and the diagnosis of CVA . The mean age of CVA was 30.5 ± 12 yrs, while the mean age of other patients was 42 ± 15 yrs (P .006).

(Table 3) Statistical Correlation findings (determined by Pearson correlation)

Feature	**CVA(n=56)**	**Others (n=13)**	**2-tailed Significance**
Age (yrs)	30.5 ±12	45.2 ± 14.8	0.006
Cough duration (weeks)	121.5±148	64 ± 74	0.239
Eosinophilia/cmm)	324±195.9	224 ± 173	0.136
Baseline FEV1(mean± SD)	72.4±2.55	72.5 ± 1.5	0.879
Post bronchodilator FEV1(mean± SD)	83.3 ± 3.3	79 ± 1.05	0.00

DISCUSSION

Out of the 69 studied patients; 39 (56.5%) were females, which is in agreement with the findings of several studies that showed higher prevalence of chronic cough among females possibly due to an intrinsically heightened cough response[10]. Eight patients (11.6%) were smokers, 7 of them were males (23.3%), and one female (2.5%). We could not be sure of the actual number of the female patients who smoked, as in Libya, smoking in females is considered as a social stigma. CVA was diagnosed in 56 out of the 69 selected patients (81.15%) (figure 2); this was a high ratio when compared with the (6-59%) ratios in other similar studies[7]. This could have been due to the use of strict selection criteria. Diurnal variations were reported in 87.5% of CVA patients (cough more sever and frequent night and or early morning). Blood eosinophilia with a mean value of 603/cmm, was detected in 15 CVA patients (26.7 %). In the western countries; mild secondary eosinophilia often represents an allergic reaction, or exposure to a variety of *drugs. In the developing* world it can also occur in parasitic infestations. During the pulmonary larval migration; patients may complain of cough, malaise, and fever, they are usually anemic and their chest radiography may show transient pulmonary infiltrates [11]. None of our CVA patients had such findings , and the drug history was negative. Sputum eosinophilia is considered as a marker of airway inflammation and was recorded in 33 of the CVA patients (58.9_%). Some studies [12] showed that asthmatics with higher sputum eosinophil count (≥ 3%) were more difficult to control with standard therapy and needed more time to achieve satisfactory FEV1 level. Personal and / or family history of atopic diseases (rhinitis, eczema, allergic conjunctivitis, and /or food allergies) was reported in 32 of the CVA patients (57.1%). Allergic rhinitis and asthma often co-exist and appear to be a continuum of airway disease. The contribution of the

PND to the chronic cough is controversial and may be difficult to establish[13,14]. Allergic rhinitis was recorded in 45 of the CVA patients (80%). None of the studied patients had findings going with "Atopic cough ". GERD is reported to be the second or third most common cause of chronic cough, (30-40%)[11,12]. In our study; only 7 (10.1 %) were diagnosed as GERD associated chronic cough. This low percentage could be explained again by using strict selection criteria**.**

In the remaining 6 (8.7%) patients, who were males & smokers, the cause of cough was not explained. Active and passive Cigarette smoking can enhance the cough response, though; smokers rarely seek medical advice specifically for cough[1]. They were prescribed bronchodilator therapy and were advised to stop smoking.

Study limitations

The cough was not assessed by the quality of life questionnaires that were recommended by the more recent European society guidelines.

It would have been better to use an objective marker for judging the CVA response to therapy; as an example, Bandyopadhyay et al suggested the use of the sputum eosinophil count for the follow up of asthmatic patients[12].

CONCLUSION

The prevalence of isolated chronic dry cough among the patients who presented to the respiratory clinic was 8.6%. CVA was the most common cause (81.15%), most of these patients (80%) had rhinitis too. 56.5% of the CVA patients were females and there was a statistical association with CVA & younger age. GERD related cough was a less prevalent cause (10.1% of total % 71.4% males). The cough in both subgroups resolved or significantly improved with the specific treatment.

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