

## ORIGINAL ARTICLES

# OCCULT FILARIA INFECTION: COULD IT BE A CAUSE OF CHRONIC DRY COUGH?

ABDUL WADUD CHOWDHURY<sup>1</sup>, AMITAV SAHA<sup>2</sup>, ZIAUR RAHMAN CHOWDHURY<sup>3</sup>, ABU SADIQUE ABDULLAH<sup>4</sup>

### Abstract:

**Background:** Management of chronic dry cough is a challenging problem for physicians. A significant proportion of patients remain undiagnosed and not cured for a long period. So this study was undertaken to identify etiology of chronic dry cough.

**Methods:** A prospective study was done in a private center, Dhaka during the period of April 2007-February, 2008 among 80 patients who were suffering from chronic dry cough for more than three months.

**Results:** 80 patients of chronic dry cough were prospectively studied on the basis of history, clinical examination and investigation reports. Among them, (41, 51.25%) were diagnosed as having usual causes of dry cough like cough variant asthma (21, 26.25%), heart Failure (10, 12.5%), sinusitis/post nasal drip (4.5%), gastro esophageal reflux disease (2, 2.5%) and drug-ACE inhibitor (4,5%). This group of patients improved after treatment of their primary cause except 6 (7.5%), who showed no improvement. These patients and the rest 39 (48.75%) patients did not have any discernible cause of chronic cough. They were evaluated by CFT for filaria. Among them, 20 cases (25%) showed moderate to strongly positive result. This CFT filaria positive group was treated with a combination of ivermectin and albendazole. Patients were followed up for up to four months. Result showed cough was totally absent in 80% treated patients with the rest 20% showing significant improvement.

**Conclusion:** This study advocates that, significant proportion of chronic dry cough patients were actually suffering from occult filaria and they responded well to treatment with drugs-ivermectin and albendazole combination.

### Introduction:

Cough is a sudden explosive force of air through the glottis in an effort to clear mucus or other matter from large bronchi, trachea or larynx. It is an important reflex mechanism protecting the airway<sup>1</sup> and most frequent symptom of respiratory disease. Any disorder resulting in inflammation, constriction, infiltration or compression of airway can be associated with cough. It can be divided into two categories: acute-lasting less than 3 weeks or chronic-lasting 3 weeks or more. The prevalence of chronic cough in the United States among non smoking adults is reported to range from 14% to 23%. It is the fifth most common symptom seen by outpatient physician and is estimated to be the primary reason for 30 million physician visits

annually.<sup>2</sup> The prevalence of chronic cough is not yet known in our country though chronic cough is commonly encountered by our physicians.<sup>3</sup> A significant proportion of these patients remain undiagnosed and not cured for a long period. Management of this group of patients is a challenging issue. This study was done to identify the etiology of chronic dry cough, which persists more than three months of duration.

### Material and methods:

It was a prospective observational study conducted in a private center in Dhaka during the period of April 2007- February 2008. A total of 80 adult patients fulfilling the inclusion and exclusion criteria were

1. Associate Professor, Department of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka.
2. Honorary Medical officer, National Institute of Chest Diseases and Hospital, Dhaka.
3. Medical Officer, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
4. Medical Officer, Department of Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka.

**Correspondence:** Dr. Abdul Wadud Chowdhury, Associate Professor, Department of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka. E-mail: drwadud@hotmail.com

enrolled in the study. Inclusion criteria were dry cough lasting 3 months or more without any significant history of occupational exposure to organic/inorganic dust, fever, haemoptysis. Exclusion criteria were patients of pulmonary TB, bronchial carcinoma and interstitial lung disease. The patients were examined thoroughly. Then following routine laboratory investigations were done-

total and differential count of WBC, Hb%, ESR, total circulating eosinophil count, sputum for eosinophil count, CXR P/A view, ECG, RBS, serum creatinine. Selective investigations like X-ray PNS OM view, upper GI endoscopy, echocardiogram-(2D/Colour Doppler), lung function test, methacholine challenge test and CFT for filaria were also done as needed.

Thus after primary evaluation, 41 patients were diagnosed as having usual causes of dry cough like cough variant asthma 21(26.25%), heart failure 10(12.5%), sinusitis/post nasal drip 4(5%), gastro-esophageal reflux disease- GERD 2(2.5%) and drug-ACE inhibitor 4(5%). The rest 39(48.75%) patients remain undiagnosed. The diagnosed group improved after treatment of their primary cause except 6(7.5%) patients. These 6 and the rest 39 patients did not have any discernible cause of persistent cough. They were then evaluated by CFT for Filaria. Among them 20 cases (6 old + 14 new) showed moderate to strongly positive result for CFT Filaria.

This CFT filaria positive group was treated with a combination of ivermectin and albendazole. Ivermectin 400ug/kg –single dose in empty stomach half an hour before meal & albendazole 400mg,twice daily for 5 days after meal. Patients were followed up for up to four months (mean 3.2 months).

**Results and observations:**

Out of 80 patients, 43(53.75%) were female and 37(46.25%) were male. Age range was 20 to 70 years with mean age 42.3 years. Most (71.25%) of the patients were between 31-50 years age group. Majority were housewife 39 (48.75%) and service holders were 17(31.25%). Among them, 13 (16.25%) were current smoker, 5 (6.25%) were ex-smoker and the rest 62 (77.5%) were non-smoker.

**Table-I**

*The presenting symptoms of study population (n=80)*

	No. of patients	Percentage %
Duration of cough	Mean 5.2 ± 0.5 months, Range 3-8 months	
Nocturnal cough	14	17.5
Severity of Cough	Mild Moderate Severe	32 39 9
		40 48.75 11.25
Diurnal/seasonal variation of cough	5	6.25
Chest pain	7	8.75
Breathlessness	10	12.5
Drug history (ACE inhibitor)	4	5
Swelling of body	4	5
History of allergy	9	11.25
Heart burn/water brash	2	2.5
Headache, nasal discharge and recurrent throat infection	4	5
Family history of asthma	6	7.5

Symptom analysis among patients (Table-I) showed 14 (17.5%) patients had nocturnal periodicity, 10 (12.5%) patients had breathlessness, 7 (8.75%) patients had chest pain, 4 (5%) patients had swelling of body, 9 (11.25%) patients had history of allergy and 4(5%) had headache.

The detailed investigation showed 11 (13.75%) patients had blood eosinophilia, 10 (12.5%) patients had sputum eosinophilia, 10 (12.5%) patients had ECG and Echocardiogram evidence of ischaemic/valvular heart disease, 2 (2.5%) patients had gastritis, 4(5%) patients had sinusitis, 21(26.25%) patients had positive methacholine challenge test.

**Table-II**

*Final aetiological diagnosis of study population*

Disease	No of Patients (n=80)	Percentage %
Cough variant asthma only	18	22.5
Heart failure only	8	10
Sinusitis	4	5
Drug (ACE inhibitor) only	3	3.75
GERD	2	2.5
Occult filaria infection	20	25
Still undiagnosed	25	31.25

Table-II showed the final diagnosis of study population- cough variant asthma 18 (22.5%), heart failure 8(10%), sinusitis 4(5%), drug- ACE inhibitor 3(3.75%), GERD 2(2.5%), occult filaria infection 20(25%) and still undiagnosed 25(31.25%).

During treatment, side effects of drugs were very insignificant. Follow up showed cough was totally absent in 16(80%) treated patients with rest 4(20%) showing significant improvement.

### Discussion:

In Bangladesh, prevalence of chronic cough is not known, though it is a commonly encountered complaint. A systematic diagnostic approach based on history, clinical examination and a number of investigations reveal the cause in most cases.<sup>4</sup> The commonest causes are PNDS (post nasal drip syndrome), asthma, GERD, chronic bronchitis and ACE inhibitor induced cough.<sup>5</sup> These conditions often coexist and may simultaneously contribute to cough. A combination of treatments are necessary for managing these cough.<sup>6</sup> Patients with chronic cough present more of a diagnostic challenge, specially those individual with a normal examination, chest X-ray and lung function studies. The main objective of this study was to identify the etiologies of chronic dry cough.

The study showed that clearly identifiable causes of chronic dry cough were present in about half of the patients (51.25%). Among the rest, 25% more were identified as cases of occult filaria infection. This finding is important because this group of patients did not show the classical features of tropical pulmonary eosinophilia.

Usually occult filariasis present with massive eosinophilia (30-80%; absolute count above 3000per/mm<sup>3</sup>), generalized lymph node enlargement, hepatosplenomegaly, pulmonary symptoms and absence of microfilaria. The syndrome has been reported mostly from India, Srilanka, South East Asia, China, Philippines, Brazil & Africa.<sup>7</sup> Tropical pulmonary eosinophilia (TPE) is a manifestation of occult filariasis and is characterized by low-grade fever, weight loss, paroxysmal cough with sputum, dyspnoea (not expiratory) and splenomegaly.<sup>7</sup> Diagnosis of TPE requires (1) history of paroxymal nocturnal dyspnoea, (2) radiographic evidence of pulmonary infiltrate, (3) peripheral blood eosinophilia greater than 3000 cell/cmm, (4) elevated serum IgE level, (5) very high level

of antifilarial antibody, (6) a rapid clinical response to antifilarial therapy with diethylcarbamazine (DEC).

In this study, our close observation showed that occult filaria infected persons complained of chronic dry cough in the absence of other significant symptoms. They, therefore, remained undiagnosed for a long period. This identified occult filaria group was treated with a combination of ivermectin and albendazole. In comparative study of ivermectin and DEC – the two drugs were found to be equally efficacious in reducing microfilaria burden.<sup>8</sup> Combination of ivermectin & albendazole is under evaluation as an alternative of DEC.<sup>9</sup> Ivermectin kills the parasite by interfering with nervous system and muscle function, in particular by enhancing inhibitory neurotransmission. The drug binds and activates glutamate-gated chloride channels (GluCl<sub>s</sub>) present in neurons and myocytes -resulting in neuro-muscular paralysis and death of parasite.<sup>10</sup> Side effects are nausea, vomiting, decreased appetite, diarrhoea or constipation, muscle or joint pain, swelling of lymph node, fever, tiredness, dizziness, itching. On the other hand albendazole is slow macrofilaricidal and microfilaricidal. Dose for microfilaria is 400mg-single dose and for macrofilaria 400mg-twice daily for 3 weeks. A comparative study using a single dose of albendazole 600 mg alone or in combination with ivermectin 400 micrograms/kg or DEC 6 mg/kg was compared with a single dose of the combination DEC and ivermectin has established the tolerability, safety and efficacy against bancroftian filariasis.<sup>11</sup> Side effects of DEC are more common & relatively serious- fever, headache, myalgia, dizziness, allergic reaction, anorexia, vomiting, urticaria, asthmatic attack, cough, chest pain etc. Close observation showed the combination of ivermectin and albendazole is cheap and less toxic. We found the same in our study. The side effects were much lower probably due to less disease burden. The dosage we have used –ivermectin 400 µg/kg- single dose & albendazole 400-twice daily for 5 days is an empirical one. But the results showed that it was very effective & well tolerated. Follow up showed this combination is effective too. However one significant finding is that at least one-third patients (31.25%) still remain undiagnosed.

### Conclusion:

In this study, we have identified that occult filarial infection is the cause of chronic dry cough in a significant number (25%) of patients. We also showed

that a combination of ivermectin & albendazole is an effective, cheap & very well tolerated regime for this group of patients. However, with all these efforts one-third patients of chronic dry cough still remain undiagnosed. Further study is therefore needed to elucidate other yet unidentified factors responsible for chronic cough.

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