Possible Effect of *Chlamydophila pneumoniae* on COPD Exacerbation

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ABSTRACT

**Background:** *Chlamydophila pneumoniae* is one of the common causative agents of respiratory infections. The present study aims to find the role of *Chlamydophila pneumoniae* infection in infectious exacerbation of chronic obstructive pulmonary disease (COPD).

**Materials and Methods:** Sixty-five nasopharyngeal swab specimens of COPD patients were studied using fluorescent antibody staining with chlamydia specific conjugated antibody and with fluorescent microscopes. Data were analyzed by using SPSS software, version 13.

**Results:** A total of 65 COPD patients (as defined by the American Thoracic Society), 53 (81.5%) males and 12 (18.5%) females were included in the study. Forty-six (70.7%) subjects had exacerbated COPD while 19 (29.3%) were stable COPD patients. We found 4 positive cases of chlamydophila infection (6.15%), 3 of which (2 men and 1 woman) belonged to the exacerbation group and 1 had stable COPD.

**Conclusion:** Data analysis revealed that there was no significant correlation between chlamydophila infection and COPD exacerbation (P= 0.848). *(Tanaffos 2008; 7(1): 63-67)*

**Key words:** Chlamydophila pneumoniae, COPD, Exacerbation

INTRODUCTION

*Chlamydophila pneumoniae*, an obligate intracellular bacterium, was first recognized as a respiratory pathogen in 1986 (1). In patients with COPD, acute bacterial infections of the respiratory tract are common and have a negative impact on quality of life and on the progression of disease, particularly in severely affected patients (2). Most of the morbidity, mortality and healthcare costs of COPD patients are related to the exacerbation of COPD which is reported to happen at an average of one to four times per year (3). Several studies have
shown that there are three bacteria which are responsible for the majority of infective exacerbations; namely, *Hemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis* (4). Previous studies evaluating the role of *C. pneumoniae* in COPD have shown the incidence of infection with the organism to be 4% and 16% in non-hospitalized and hospitalized patients, respectively (2). Chronic *C. pneumoniae* infection has been found to be common in chronic bronchitis and could contribute to disease progression by a toxic effect on bronchial epithelial cells, impairing ciliary function, and increasing chronic inflammation via proinflammatory cytokine production (5).

While serological analysis represents the current routine method for the diagnosis of *C. pneumoniae* infection, the "gold standard" at the moment is the microimmunofluorescence assay (MIF). Other immunological tests such as antigen detection with use of conjugated antibody (DFA) are also valuable (6). While there has been numerous studies regarding the role of *C. pneumoniae* infection in COPD exacerbation (1,2,5,7,8,9) utilizing immunological analysis as their method of diagnosis, few are conducted using DFA. In this study we tried to identify the role of *C. pneumoniae* infection in the exacerbation of COPD using the DFA method.

**MATERIALS AND METHODS**

This cross-sectional study was conducted on COPD patients who were admitted to Loghman Hakim and Masih Daneshvari Hospitals in Tehran from September 2005 to October 2006. After obtaining an informed consent, patients were divided into the case (exacerbated) and the control (stable) groups based on the definitions used by the "American Thoracic Society". A nasopharyngeal swab was obtained from each patient and the specimens were placed on microscope slides and taken to our laboratory. Following their preparation, the specimens were studied for specific *Chlamydia pneumoniae* antigen using direct fluorescence antibody assay (DFA) based on the DFA kit instructions.

Once the patient’s specimen was collected, the slides were marked with the patients name and/or ID. The swab was then lightly rolled onto the slide and fixed immediately. After the specimen was air dried (2-3 minutes) it was transported to the laboratory. The slides were then stained with a fluorescent-labeled antibody specific for chlamydia. The antibody conjugate binded specifically to any chlamydia presented in the specimen. A rinse step removed unbound antibody. When slides were viewed under a fluorescence microscope, chlamydia positive specimens contained apple-green elementary bodies contrasted by the red background of the counterstained cells.

The collected data was analyzed using SPSS software version 13, chi-square and t-tests. P<0.05 was considered significant.

**RESULTS**

Sixty-five COPD patients (53 males, 81.5%, 12 females, 18.5%) with a mean age of 65.7±12.9 yrs., were included in this study. Three patients in the exacerbated group (6.5%) and 1 in the stable group (5.3%) were positive for *C.pneumoniae* (p=0.848) which constituted a total number of 4 patients (6%). One (8.3%) of 12 females and 3 (5.7%) of 53 males were positive for *C. pneumoniae* (p=0.728). The mean age of patients who were positive and negative for *Chlamydia pneumoniae* was 52.67±17.039 and 66.45±12.485 yrs., respectively.

From all 65 patients, 46(70.7%) had exacerbated status (42 males, 4 females) and 19 were stable (11 males, 8 females). The mean age of patients in the stable and the exacerbated group was 62.74±12.5 and 67.24±13.0 yrs respectively (Table 1).
Table 1. Results of under study population.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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Exacerbation status

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<td>stable</td>
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<tr>
<td>Total</td>
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Chlamydia infection

<table>
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<tr>
<td>negative</td>
<td>61</td>
</tr>
<tr>
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DISCUSSION

The prevalence of *C. pneumoniae* infection depends on the subject’s age, geographic area of residence and the presence of other chronic diseases. *C. pneumoniae* infection in Asia has been reported to be more endemic than in western countries (3). Smoking has been proposed as a potential confounder in epidemiologic studies of *C. pneumoniae* infection (10).

An IgG antibody prevalence rate of about 23% in the first age class is consistent with an early exposure to *Chlamydia pneumoniae* infection in the community (12). While the seroprevalence rates do not differ significantly according to sex, the prevalence rates seem to increase with age (12). *Chlamydia pneumoniae* infection had no association with age or sex in this study.

Exacerbations punctuate the course of COPD in many patients (13). It is perhaps surprising that there is no consistently used definition of acute exacerbation of COPD (AECOPD), either in clinical practice or in research. However, recently a consensus statement defined exacerbation as "a sustained worsening of the patient’s condition, from the stable state and beyond normal day to day variations that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD (14). Addressing the issue of whether bacteria increase during exacerbations requires prospective studies that examine the bacteriology of the sputum in the same cohort of patients during both remission and exacerbation(13). With this in mind bacteria are estimated to be responsible for approximately half of all cases. *H. influenzae, M. catarrhalis, S. pneumoniae* and *C.pneumoniae* are the most important causes of acute exacerbation of bacterial origin; although, the incidence of *C. pneumoniae* in patients with acute exacerbations of chronic bronchitis appears to vary considerably from as low as 4–5% to >30% (1). In this study 6.5% of patients with exacerbation of COPD were positive for *C. pneumoniae*.

The diagnosis of acute *C. pneumoniae* infection is usually based on serologic criteria that include the presence of IgM antibodies and/or a four-fold rise in IgG antibody titers(2). The absence of an increase in IgM suggests reinfection rather than primary infection. Reinfection or reactivation of chlamydiophilal infection is followed by elevated IgG antibody levels that persist for months or years, whereas IgA levels decay much more rapidly. For this reason, IgA antibody is considered a more reliable marker for chronic chlamydiophilal infection (10).

Most of the studies conducted on the potential role of *C.pneumoniae* infection in COPD exacerbation have used the above-mentioned
serologic criteria for the diagnosis while MIF is recommended as the only reliable serological test available in commercial kits (5).

There are numerous studies confirming the role of *Chlamydophila pneumoniae* infection in COPD exacerbations, as detected serologically (2,3,7, 8, 15, 16, 17 ) while there are others which vote against it (4,5, 9, 10, 11). But almost all of these studies used antibody titers for detection of the organism which is not the method of choice for this purpose. In our study there was no association between COPD exacerbation and *C.pneumoniae* infection. We recommend a more cautious interpretation of the results of the studies which can find such an association until more research is done on the subject using the MIF method.

We had some drawbacks in our study, the most important of which was the total number of control group as well as the test subjects. A larger number of specimens could have made the results more accurate.

Thus, we recommend a larger study with more cases in both groups using DFA as the diagnostic method for better and more valid conclusions.

**Acknowledgement**

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**REFERENCES**


