

Infection with *Mycoplasma pneumoniae* is not related to asthma control, asthma severity, and location of airway obstruction

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Background: *Mycoplasma pneumoniae* is an organism that reportedly has a strong relationship to asthma. However, asthma severity and location of airway obstruction have not been compared between asthmatic patients with and without evidence for remote mycoplasma infection.

Objectives: The aim of this research was to study the relationship between previous *M. pneumoniae* infections in asthmatic patients and presence of any predilection for the involvement of central or peripheral airways, the severity of the disease, and asthma control.

Methods: Sixty-two patients with asthma were assessed by a validated asthma control test (ACT). All patients underwent spirometry and lung volume studies by body plethysmography. The forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC) were measured. An oropharyngeal swab was obtained for polymerase chain reaction analysis to detect the mycoplasma antigen. Moreover, blood samples were obtained to measure the titration of antimycoplasma immunoglobulin M (IgM) and IgG antibodies. The asthmatic patients with a positive IgG for mycoplasma and negative PCR and negative IgM antibody were considered to have remote history of mycoplasma infection. The relationship between the asthma control using ACT score and pulmonary function variables were compared in patients with and without evidence for remote mycoplasma infection.

Results: The incidence of postnasal drip was higher among the patients with asthma who had no evidence for remote mycoplasma infection (61.3% vs 32%, $P = 0.035$). The median ACT score was 16.5 (11–22) and 20 (13.75–24) in patients with and without remote *M. pneumoniae* infection, respectively ($P > 0.05$). In addition, the medians of the predicted values of the pulmonary function test parameters (FEV₁, FEV₁/FVC, FRC, FRC/TLC, RV/TLC, maximal mean expiratory flow 25%–75%, forced expiratory flow [FEF] 50%, and FEF 75%) and actual values of 5 Hz and 20 Hz resistance were not different between asthmatic patients with and without evidence of mycoplasma infection ($P > 0.05$).

Conclusions: The present study revealed that the asthma control status and parameters of lung function tests did not differ between asthmatic patients with and without evidence of chronic *M. pneumoniae* infection. The latter indicates the similar location of airway obstruction and comparable severity of asthma between the two groups.

Keywords: *Mycoplasma pneumoniae*, asthma, asthma control test, airway, pulmonary function test

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Introduction

Asthma is a chronic disease characterized by variable airway obstruction. Allergic and immunologic factors are deemed to play a cardinal role in the pathogenesis of asthma. Recently, imbalance between type 1 and type 2 T-helper lymphocytes (TH) is believed

to play a major role in development of this disease.¹ Factors involved in asthma pathogenesis predispose the individual to increased differential overproduction of TH2 cells versus TH1 cells.² Accordingly, a number of infections have been considered to be involved in generation of asthma. For instance, mycoplasma is an organism reportedly having a strong relationship to asthma.³

On the other hand, asthma is a disease of varying phenotypes among different individuals and in different times in the same individual. The severity of asthma is believed to be linked to the location of the airway inflammation; asthma is more severe and persistent in those with functional and pathological evidence of small peripheral airways involvement compared to the central airways involvement.⁴ The aim of the present study was to investigate the relationship between previous *Mycoplasma pneumoniae* infections in asthmatic patients and presence of any predilection for the involvement of central or peripheral airways, the severity of the disease, and asthma control.

Methods

Sixty-two patients with asthma were enrolled after sequential random selection after diagnosis of asthma in a pulmonary subspecialty clinic by a pulmonologist on the basis of the American Thoracic Society guideline for diagnosis of asthma. After full history taking, physical examination, and assessment of the asthma control by asthma control test (ACT),⁵ all patients underwent spirometry and lung volume studies by body plethysmography using Jaeger body-plethysmograph (Jaeger, Wuerzburg, Germany). The forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC) were measured, and their ratios and percent predicted values for the individual were calculated. Patients with history of smoking, respiratory infection within the past 2 months, known cardiac disease, congestive heart failure, chronic respiratory disease, or any other condition affecting the lung function were excluded from study. A throat swab sample was obtained from all patients for polymerase chain reaction (PCR) analysis to detect the mycoplasma antigen. Moreover, blood samples were obtained from the patients to measure the titration of antimycoplasma immunoglobulin M (IgM) and IgG antibodies (antimyc-IgM and antimyc-IgG, respectively) using enzyme-linked immunosorbent assay (EUROIMMUN Inc, Padova, Italy). The asthmatic patients with a positive IgG for mycoplasma and negative PCR and negative IgM antibody were considered to have remote history of mycoplasma

infection. The relationship between the asthma control using ACT score and pulmonary functional variables including the values for FEV₁, FVC, RV, TLC, FRC, maximal mean expiratory flow (MMEF) 25%–75%, forced expiratory flow (FEF) 50% and 75%, and resistance (5 and 20 Hz) and their predicted values were analyzed and compared in patients with and without evidence for remote mycoplasma infection.

To achieve a power of 80% with a type 1 error rate of 0.05, the sample size was calculated as 31 patients for each group.⁶ Data are presented as median (interquartile range) or percentage. Statistical analysis was performed with SPSS for Windows (version 16.0; SPSS Inc., Chicago, IL) by using χ^2 test, Fisher's exact test, and Mann–Whitney *U* test wherever appropriate. $P < 0.05$ was considered statistically significant.

Results

Sixty-two asthmatic patients were recruited. Four patients were excluded due to positive antimyc-IgM and/or positive PCR for *M. pneumoniae*. Data from 58 patients were, therefore, analyzed. There were no differences in gender, age, and incidence of cough, sputum, wheezing, dyspnea, gastroesophageal reflux, and history of atopy between the groups (Table 1, $P > 0.05$). Among different respiratory symptoms of asthma, the incidence of postnasal drip (PND) was higher among the patients with asthma who had no evidence for remote mycoplasma infection (61.3% vs 32%, $P = 0.035$, Table 1). The median ACT score was 16.5 (11–22) and 20 (13.75–24) in patients with and without remote *M. pneumoniae* infection, respectively (Mann–Whitney *U* test, $P > 0.05$, Table 1). In addition, the medians of the predicted values of the pulmonary function test parameters (FEV₁, FEV₁/FVC, FRC, FRC/TLC, RV/TLC, MMEF 25%–75%, FEF 50%, and FEF 75%) and actual values of 5 Hz and 20 Hz resistance were not different between asthmatic patients with and without evidence of mycoplasma infection (Mann–Whitney *U* test, $P > 0.05$, Table 2).

Discussion

An association of asthma with mycoplasma infection has been believed and investigated by several researchers in the past. *M. pneumoniae* may precede the onset of asthma, exacerbate asthma, or play a part in asthma chronicity.^{7,8} Such an association has been demonstrated earlier by isolation of *M. pneumoniae* in oropharyngeal swabs and serologic assessments and later by lower airway evaluations.^{9,10} Previous studies on patients with chronic asthma revealed that mycoplasma infection was more frequent in asthmatic

Table 1 Demographic data and symptom frequencies in asthmatic patients with and without remote mycoplasma infection

	With remote mycoplasma infection (n = 26)	Without remote mycoplasma infection (n = 32)	P value
Gender (male/female)	13/13	15/17	1.00
Age (years)	38.5 (29.5–44.25)	38 (29–44.75)	0.83
Cough: n (%)	21 (80.8%)	28 (87.5%)	0.71
Sputum: n (%)	11 (42.3%)	18 (58.1%)	0.29
Wheezing: n (%)	22 (88%)	22 (73.3%)	0.31
Dyspnea: n (%)	20 (76.9%)	25 (78.1%)	1.00
Gastroesophageal reflux: n (%)	5 (20%)	9 (29%)	0.54
Postnasal drip: n (%)	8 (32%)	19 (61.3%)	0.03*
History of atopy: n (%)	9 (34.6%)	11 (34.4%)	1.00
ACT score	16.50 (11–22)	20 (13.75–24)	0.06

Note: *P < 0.05.

Abbreviation: ACT, asthma control test.

individuals.^{9–11} Nonetheless, Tuuminen et al found no significant difference in *M. pneumoniae* serology between asthmatic patients and control group.¹² In the present study, we aimed to study the relationship between previous *M. pneumoniae* infections in asthmatic patients and presence of any predilection for the proximal or distal airways involvement, the severity of the disease, and asthma control.

The present study revealed no significant difference in the asthma control status assessed by ACT between asthmatic patients with and without evidence of chronic mycoplasma infection. In addition, various parameters of lung function tests, including tests sensitive to central as well as peripheral airway obstruction, did not differ between the two groups, indicating similar involvement of central and peripheral airways as well as comparable severity of asthma. Moreover, among different respiratory symptoms of asthma, the incidence of PND was higher among the patients with asthma who had no evidence for remote mycoplasma infection. To the best of our knowledge, the present study is the first investigation to compare the asthma severity and

location of airway obstruction in asthmatic patients with and without evidence for remote mycoplasma infection.

Severity of asthma is measure as the difficulty in controlling asthma with treatment after excluding amendable factors.¹³ On the other hand, asthma control reflects the patient's current clinical status as well as the future risk of adverse outcomes.^{13,14} Following the evidence revealing an association between achievement of good asthma control and improved health status,¹⁵ the level of asthma control rather than the disease severity is highlighted more in guideline-based asthma treatment protocols.¹³ In the present study, we found no difference in pulmonary function tests, indicative of the asthma severity, in those asthmatics with and without chronic mycoplasma infection.

Severe asthma has been attributed to more involvement of small (distal) airways rather than proximal airways.⁴ Interestingly, Balzar et al reported a relationship between chymase-positive mast cells in the distal airways and pulmonary function tests in severe asthma.¹⁶ In the present study, to determine the location of airway obstruction in asthmatic

Table 2 Pulmonary function test parameters in asthmatic patients with and without remote mycoplasma infection

	With remote mycoplasma infection (n = 26)	Without remote mycoplasma infection (n = 32)	P value
FEV ₁ (% predicted)	72.60 (51.92–88.90)	76.65 (53.15–89.27)	0.80
FEV ₁ /FVC	68.60 (62.40–74.05)	70.35 (63.45–80.55)	0.37
FRC (% predicted)	93.15 (82.22–109.50)	93.90 (74.40–105.50)	0.67
FRC/TLC (% predicted)	99.95 (84.40–127.50)	98 (85.4–120)	0.71
RV/TLC (% predicted)	108 (92.02–152)	113 (88.25–139.25)	0.92
MMEF 25%–75%	33.75 (23.07–52.50)	40.55 (21.27–70.02)	0.55
FEF 50% (% predicted)	40.50 (24.47–57.60)	44.60 (23.75–70.67)	0.73
FEF 75% (% predicted)	29.55 (19.20–43.47)	32.55 (20.75–54.35)	0.70
Resistance (5 Hz) (kpa/L/sec)	0.67 (0.39–0.91)	0.55 (0.39–0.82)	0.66
Resistance (20 Hz) (kpa/L/sec)	0.35 (0.23–0.51)	0.36 (0.28–0.42)	0.92

Abbreviations: FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; FRC, functional residual capacity; TLC, total lung capacity; RV, residual volume; MMEF, maximal mean expiratory flow; FEF, forced expiratory flow; Hz, Hertz; kpa, kilopascal; L, liter; sec, second.

patients with and without remote mycoplasma infection, parameters of pulmonary function test (indicative of both central and peripheral airway function) were compared. However, no superiority of either distal or proximal airways involvement was noted between these two groups. Consistent with our results, Teig et al found no correlation between positive PCR for *M. pneumoniae* and FEV₁, the only reported parameter in their study, in 26 children with stable asthma.¹⁷ A few investigations on a relation between *Chlamydia pneumoniae* and severity of pulmonary obstruction in asthmatic patients exist in the literature. Huittinen and colleagues concluded that *C. pneumoniae* heat-shock protein 60 IgA antibodies were inversely associated with FEV₁.¹⁸ Similarly, Black et al reported an inverse association between IgG antibodies to *C. pneumoniae* and FEV₁.¹⁹

In conclusion, the asthma control status and parameters of lung function tests did not differ between asthmatic patients with and without evidence of chronic *M. pneumoniae* infection. The latter indicates the similar location of airway obstruction and comparable severity of asthma between the two groups. Further investigations with larger sample size and focusing on both *M. pneumoniae* and *Chlamydia pneumoniae* are needed to strengthen the present findings.

Disclosure

The authors report no conflicts of interest in this work.

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