# Antichlamydia IgG Antibody in Adult Asthmatics in Al-Najaf

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***Received: 16 Aug. 2019; Accepted: 28 Nov. 2019***

**Abstract-** Infection is presumed to have a rule in the promotion of asthma exacerbations, and in deterioration of the course of the disease, Chlamydia pneumoniae (C. pneumoniae) is claimed to be a possible cause for these two issues. To assess the positivity and the titer of C. pneumoniae IgG antibodies in relation to the state of asthma and its severity. 61 asthmatic patients aged 15-85 years (mean of 47.10±14.887), and 29 apparently healthy, nonasthmatic age and gender-matched volunteers (control group) were assessed as at Asthma and Allergy Clinic in Al-Sader Medical City in AL-Najaf province, Chlamydia Pneumoniae IgG ELISA Kit was used for the detection of IgG antibody to C. Pneumoniae in human serum to detect chronic infection, and Spirometric test was done, and the best results for FEV1 and PEFR were taken. IgG antichlamydial antibodies were positive in 21 (34.4%) of patients compared to 4 (13.8%) of controls, and the difference was significant with OR=3.281, the seropositivity in acute exacerbation was more than in stable asthmatic, 43.8% vs. 24.1% (*P*=0.029), seropositivity was nonsignificantly more in moderate and severe asthma as compared with mild asthma, a significant inverse correlation between IgG titer and pulmonary function test parameters (FEV1, PEFR) was observed as the FEV1 & PEFR values decrease with increase IgG titer. Chronic C. pneumoniae infection is common in adult asthmatics and correlated with exacerbations & increased severity and disturbed lung function.



*Acta Med Iran* 2020;58(1):32-37.

**Keywords:** Asthma; IgG antichlamydial; Spirometry; FEV1; PEFR

## Introduction

Asthma is a common chronic inflammatory disease of the airways characterized by recurrent episodes of wheezing, chest tightness, and cough, these symptoms are caused by widespread, but variable airflow limitation that is partially or completely reversible, the recovery of the airway obstruction is either spontaneous or by medication (1).

The prevalence of asthma had been increased in most areas of the world, in USA asthma affected more than 8% of children and adults in 1996, doubling the incidence observed at 1980 according to National Health Interview Survey (NHIS) Data and the rise in incidence is still ongoing (2), the same process is observed in developing countries and urbanization may be an important contributing factor (3,4).

The hygiene hypothesis, which provided an evidence that exposure of young children at home to older children is a protecting factor against development of asthma and also other atopies in childhood had got a lot of concerns, many studies supported this concepts where there is inverse relationship between intense systemic childhood infection and development of asthma (5,6), on the other hand early childhood infection with respiratory syncytial virus had been linked with increased incidence of asthma in childhood, many long term studies of children admitted to hospital with documented RSV showed that approximately 40% will continue to wheeze or have asthma into later childhood (7,8), another important pathogen, Chlamydia pneumonia (C. pneumoniae) has been claimed in the persistence of asthma and increase in severity of symptoms during acute attack, Cunningham et al in a large scale study revealed that the level of antibodies (IgG) in nasal aspirate was seven time in those with four exacerbation as compared to those who have one exacerbation and these antibodies persists more with repeated assessment pointing p to chronicity of infection of C.pneumoniae, the levels of antibodies was correlated

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with the severity of asthma (9), also Black PN et al found that forced expiratory volume in one second (FEV1), and peak flow rate had inverse association with the level of C.pneumoniae specific IgG antibodies and higher levels of antibody were associated with higher daytime symptoms (10).

**Aim of the study**

To assess the role of C.pneumonia infection in asthma exacerbation and severity.

## Materials and Methods

**Subjects**

The study was carried out from February 2018 till august 2018, 61 patients with bronchial asthma who attended Asthma and Allergy clinic in Al-Sader Medical City in AL-Najaf province were included, and their ages ranged from 15-85 years with a mean of 47.10±14.887.

Age, gender, occupation, residency, age of onset and duration of disease, the frequency and severity of exacerbations, family history of similar or other allergic conditions, history of chronic disease, smoking, and drug history were taken.

Exclusion criteria: current acute infection, tuberculosis, and other lung disease diseases.

The Control group consisted of 29 healthy, nonasthmatic volunteers; the mean age was 20-62 years with a mean of 41.34±12.55, age, gender, residency, and occupation were matched with the patients' group (Table 1).

**Table 1. Demographic and clinical characters of the studied group**

| Variables | | Patients (N=61) | Control (N=29) | *P* |
|---|---|---|---|---|
| **Age(yrs)** | | 47.10±14.887 | 41.34± 12.556 | .076 |
| **Gender** | **Male** | 29(47.5%) | 12(41.4%) | 0.583 |
| | **Female** | 32(52.5%) | 17(58.6%) | |
| **Residency** | **Urban** | 38(62.3%) | 21(72.4%) | 0.345 |
| | **Rural** | 23(37.7%) | 8(27.6%) | |
| **Smoking** | | 35(57.4%) | 12(41.4%) | 0.156 |
| **Positive allergic history** | | 49(80.3%) | 4(13.8%) | .0001 |
| **FEV1** | | 46.51±18.444 | 55.76±15.364 | 0.022 |
| **PEFR** | | 44.10±18.263 | 53.48±17.701 | 0.024 |
| **Clinical state** | **Stable** | 29(47.5%) | -- | -- |
| | **Acute exacerbation** | 32(52.5%) | -- | -- |

All participants (patients and control) were from Al-Najaf province, and they have been instructed and informed about the aim of the study, and test procedures and their acceptances were taken.

Asthma severity was assessed according to GINA classification into Mild asthma: Well-controlled with short-acting bronchodilators alone or with low-dose inhaled corticosteroids (ICSs) or leukotriene antagonists.

Moderate asthma: Well-controlled with low-dose ICS/long-acting beta2-agonists (LABA).

Severe asthma: Needing high-dose ICS/LABA (1).

**Method**

**Sample collection**

Blood samples of 3 ml were collected. The Cal biotech Chlamydia Pneumoniae IgG ELISA Kit (CP083G) is used for the detection of IgG antibody to C. Pneumoniae in human serum to detect chronic infection. A cut-off value was 0.9-1.1, according to kit instructions. Samples below 0.9 were regarded as negative.

**Lung function test**

Spirometric tests done by using the SPM (Contec Medical System) spirometer and performed according to a standardized protocol of well-validated and widely accepted criteria and the equation for calculating the predicted value were those adopted by the European respiratory society (Miller *et al*., 2005).

**Statistical analysis**

Statistical analysis was done by using the statistical package for social sciences (SPSS) version 22, 2014. Statistical analysis was performed using t-test, chi-square tests, and Pearsons correlation (r). *P* set at ≤0.05 was considered as the significant difference

## Results

**Characteristics of subjects**

The main demographic, clinical, and other relevant features of both asthmatic and control groups were comparable, and there were no significant differences in

such factors such as age, gender, residency & smoking (Table 1).

Patients exhibited highly significant differences from the control group for family history of allergy, history of admission to hospital in the last three months, and results of pulmonary function test.

**Antichlamydia antibodies among studied groups**

Results of IgG antichlamydial antibodies were positive in 21(34.4%) of patients compared to 4(13.8%) of controls; the difference was significant with OR=3.281 (Table 2). Also, the seropositivity of antichlamydial antibodies in acute exacerbation was more than in stable asthmatic, 43.8% versus 24.1%, respectively, but the difference was nonsignificant (*P*=0.1074), (Table 3).

**Table 2. Seropositivity of IgG antichlamydial antibodies among asthmatic patients versus control**

| antichlamydial IgG Antibody | Asthmatic (N=61) | Control (N=29) |
|---|---|---|
| **Positive** | 21(34.4%) | 4(13.8%) |
| **Negative** | 40(65.6%) | 25(86.2%) |
| **Total** | 61(100%) | 29(100%) |

*P*=0.041, OR=3.281

**Table 3. Seropositivity of IgG antichlamydial antibodies among stable asthmatic and acute exacerbation**

| antichlamydial IgG antibody | Stable (N=29) | Acute exacerbation (N=32) | Control (N=29) |
|---|---|---|---|
| **Positive** | 7 (24.1%) | 14(43.8%) | 4(13.8%) |
| **Negative** | 22 (75.9%) | 18(56.2%) | 25(86.2%) |
| **Total** | 29(100%) | 32(100%) | 29(100%) |

*P*=0.1074 Non significant difference between stable and acute exacerbation group
*P*= 0.3114 Non significant difference between stable and control group
*P*=0.0104 a significant difference between acute exacerbation and control group

**Association of IgG antichlamydial seropositivity with asthma severity**

Table 4 revealed that antibody seropositivity was more in moderate and severe groups as compared to mild asthma (35%, 50% versus 31%); however, the difference was statistically not significant (*P*=0.598).

**The relationship between Anti-chlamydia IgG titer and pulmonary function test parameters**

Figure 1 and figure 2 show a significant inverse correlation between IgG titer and pulmonary function test parameters (FEV1, PEFR) as the FEV1 & PEFR values decrease with increase IgG titer.

**Table 4. The distribution of IgG antichlamydial antibodies in the asthmatic patients according to their severity**

| antichlamydia IgG Antibody | Mild | Moderate | Severe | Total |
|---|---|---|---|---|
| **Positive** | 8(31%) | 11(35.5%) | 2(50%) | 21(34.4%) |
| **Negative** | 18(69%) | 20(64.5%) | 2(50%) | 40(65.6%) |
| **Total** | 26(100%) | 31(100%) | 4(100%) | 61(100%) |

*P*= 0.468 Non significant difference between moderate and severe groups compared with mild group

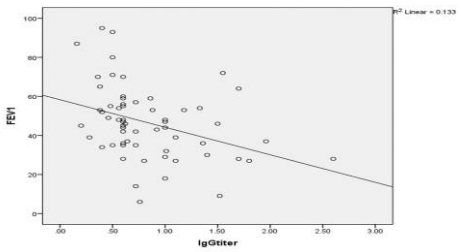


**Figure 1.** Pearson correlation between antichlamydia IgG Ab titer and FEV1. *P*= 0.004. A significant decline of FEV1(Forced Expiratory Volume in the first second ) with increasing IgG Ab titer

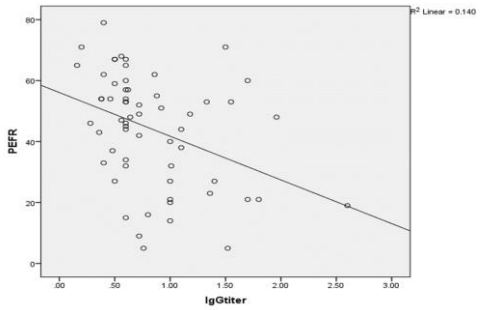


**Figure 2.** Pearson correlation between antichlamydial IgG Ab titer and PEFR *P*=0.003. A significant decline of PEFR(Peak Expiratory Flow Rate ) with increasing IgG Ab titer

## Discussion

This study is a case-control study; the main demographic features of both asthmatics and control groups were comparable, and there were no significant differences regarding age, sex, residency & smoking (Table 1).

The study demonstrated seropositivity of antichlamydial IgG in 34.4% of asthmatics patients versus 13.8% in the control group, the difference was significant (*P*=0.041, OR=3.2) and this result is consistent with that of many investigators, in Biscione *et al.*, 22% asthmatic versus 9% normal participants had a positive antichlamydial IgG (12), Specjalski and Jassem reported more than 60% of asthmatics were seropositive for antichlamydial IgG (13) however Gencay & Roth reported lower figures of seropositivity in asthmatics but still with a significant difference from the control (18.2% versus 3.0%, *P*<0.01) (14).

Chlamydia infection is difficult to be eradicated. Moreover, the immune response may cause greater inflammation, tissue injury, and consequently a variable degree of fibrosis (15), this study showed the presence of chronic Chlamydia infection in acute exacerbation more than the stable state, the results are in agreement with Carr & Kraft who demonstrated that chronic Chlamydia infection is connected with exacerbation and poor asthma control and management (16), also Webley & Hahn reported that finding (17). Additionally, Nambu *et al.*, and Yoshinari Endo *et al.*, documented that severe acute Chlamydia infection to be the cause of acute severe asthmatic attack with HRCT scan changes in a previously nonasthmatic individual, the Chlamydia infection was ascertained by paired serology (18,19), Iramain *et al.*, reported that antichlamydial pneumonia IgM is significantly prevalent among severe exacerbations than stable asthma while there was no significant difference in IgG between both group or even healthy control and concluded that acute infection trigger asthma (20), also in Iran, Ahmadi *et al.*, suggested that positive results of chlamydia culture are associated with both chronic stable and acute exacerbation of asthma (21).

In this study Chlamydial seropositivity increased with increasing severity of asthma, as chronic C. pneumoniae present in 35.5% and 50% of patients with moderate and severe asthma compared with (31%) of mild asthma, however, the observed difference was statistically insignificant, the sample size of the study may contribute. Nevertheless, many studies reported a strong significant association between chronic Chlamydia pneumoniae infection and asthma severity (22,23,24).

Hahn *et al.*, claimed that exposure to bacterial allergen enhances severe disease and reported that Chlamydia pneumoniae IgE is significantly associated with asthma & asthma severity and recommended its use as a biomarker for infectious asthma (23), also and more Earlier Hahn *et al.*, presumed this association is attributed to exposure to interleukins especially IL6 & chlamydial heat shock protein which cause hyperreactivity & inflammation (25).

This study confirmed the significant negative correlation of FEV1 & PEFR and antichlamydial IgG titer, the result was consistent with Pasternack *et al.*, in a longitudinal study that identified an accelerated decrement in lung function in the presence of chronic C. pneumoniae infection (26) also the current finding is supported by the results of interventional studies that used Clarithromycin in *C. pneumoniae* positive asthmatics, as there is a reported improvement in pulmonary function indices as FEV1and PEFR (27).

In 2013 Reiter *et al.*, in meta-analysis study showed positive effects on peak expiratory flow rate but not on forced expiratory flow rate in 1 s (FEV1) (28) but later, Kew *et al.*, demonstrated that macrolide treatment

improves FEV1 as well (29), others, like Teig *et al*., showed no such association between FEV1 & chronic C. pneumoniae infection (30), however, the study population were asthmatic children and with time such association may become more clear & sensible. Kraft *et al*. found that the improvement in FEV1 was associated with a decrease in proinflammatory cytokines like TNF-a, IL-12 and IL-5 which secreted at site of Chlamydia pneumoniae infection because of the immune response against it and these cytokines were accused of causing immune pathological tissue injury and deterioration in lung function among asthmatics (27).

1. Chronic Chlamydia pneumoniae infection is common in adult asthmatics and correlated with exacerbations & increased severity and disturbed lung function.

2. Trial of antichlamydial antibiotics in acute exacerbation & severe asthma that is difficult to control to improve patients' status.

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