CHRONIC CHLAMYDIA PNEUMONIAE INFECTION AND BRONCHIAL ASTHMA: IS THERE A LINK?

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Abstract

Purpose: Besides well-defined environmental causes, accumulating evidence suggests that respiratory tract infections play an important role in the pathogenesis of asthma. Among these Chlamydia pneumoniae infection has been discussed as possibly inducing the development of asthma. Methods: This study was designed to investigate the presence of anti chlamydial IgG, IgA, and IgM antibodies by ELISA in serum samples of 60 adults with a clinical history of asthma and 100 healthy age and sex matched controls. All the samples positive for Chlamydia genus specific IgG antibodies were then subjected to Chlamydia pneumoniae species specific IgG antibody ELISA. Results: The IgG anti chlamydial antibody-positivity rate in the patients with bronchial asthma (80%) was significantly higher in all age groups than that in the healthy age and sex matched controls (59%). No significant association was observed for IgA and IgM anti chlamydial antibodies. C. pneumoniae species specific IgG antibody seroprevalence was also found to be significantly higher in all age groups in comparison to controls (61.66% vs 38%). Conclusions: Serological evidence of chronic infection with C. pneumoniae was more frequent in patients with asthma compared with control subjects. Our results support the correlation of bronchial asthma and chronic infection with C. pneumoniae in Indian population.

Key words: Bronchial asthma; Chlamydia pneumoniae, serology, correlation

Asthma is an inflammatory disease of the airways, with a worldwide unexplained increasing incidence. Marked inflammation of the bronchial mucosa is a common feature of asthma and leads to structural changes of the lung tissue. Multiple risk factors are discussed to contribute to the development of asthma in patients with underlying atopy. Chlamydia pneumoniae has been discussed as a possible cofactor causing chronic obstructive pulmonary disease (COPD) and asthma. An association of Chlamydia infection with asthma was first described in the early 1990s[1] and epidemiological and clinical data support the suggestion that C. pneumoniae infection may partly explain the increased incidence of asthma.

Since the 1970s an increase in C. pneumoniae infection with a novel Chlamydia species, TWAR, recently named Chlamydia pneumoniae, was correlated with an increase in asthma in Finland.[2] Over the same time period an increase in asthma prevalence was also observed in other countries.[3,4] Acute C. pneumoniae infection can initiate[1,5] and exacerbate[6,7] asthma and persistent infection may contribute to chronic asthma symptoms in some patients.[5] These associations were determined by seroepidemiologic observations, case series, isolation or direct detection of the organism in specimens, successful response to antichlamydial antibiotics, or a combination of these methods.[8]

This study was undertaken to determine seroprevalence of chlamydial antibodies in general Indian population and to study association of chronic C. pneumoniae infection with bronchial asthma.

Materials and Methods

The study was designed as a case control study and was conducted in a large referral hospital providing tertiary level care to patients from all over India. Study population comprised of 60 clinically diagnosed patients of bronchial asthma admitted or attending OPD with or without exacerbation. Hundred healthy individual of both sexes selected randomly after matching for age and sex were taken as control.

Serum samples from all patients with asthma and control subjects were collected and stored at -20° C until analysis. All serum samples were first evaluated for Chlamydia genus specific IgM, IgG and IgA antibodies by respective commercially available ELISA kits (Novum Diagnostica, Germany). Since only anti chlamydial IgG antibody seroprevalence was found to be significantly high in study group in comparison to control group, all the samples positive for Chlamydia genus specific IgG antibodies were then subjected to Chlamydia pneumoniae species specific IgG antibody ELISA ( Savyon Diagnostics Ltd., Israel). Positive results were taken as indication of C. pneumoniae infection.

The results obtained were analysed statistically using Chi-square test.

Results

The seroprevalence of Chlamydia genus specific IgG,
IgA and IgM antibodies in the control group was found to be 59%, 24% and 12% respectively, with increase in seropositivity of IgG and IgA anti chlamydial antibodies with increasing age (Table 1).

Amongst the bronchial asthma group, overall seroprevalence of Chlamydia genus specific IgG antibodies was found to be 80% in comparison to 59% in age and sex matched control group. When the values in different age groups were compared, the prevalence was found to be significantly high in all the age groups (Fig.1). The odds ratio was 2.78 (95% confidence interval, 1.31 to 5.87; p value= 0.006) for seropositivity of Chlamydia genus specific IgG antibodies in patients with bronchial asthma than in similar control subjects. However, no significant difference was observed for IgA and IgM chlamydial antibodies between study and control groups (Table 2).

Chlamydia pneumoniae species specific IgG antibody seropositivity was also found to be significantly high in all age groups in comparison to age and sex matched controls (Fig. 2). Overall seroprevalence of Chlamydia pneumoniae species specific IgG antibodies being 61.66% in genus specific IgG positive study group in comparison to 38% in control group (Table 3). The odds ratio was 2.62 (95% confidence interval, 1.36 to 5.07; p value=0.0035) for

![Figure 1: Seropositivity of Chlamydia genus specific IgG antibodies in bronchial asthma vs control group](image1)

![Figure 2: Chlamydia pneumoniae IgG seropositivity in bronchial asthma vs control group](image2)

**Table 1: Seroprevalence of Chlamydia genus specific antibodies in control group**

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>IgG</th>
<th></th>
<th>IgM</th>
<th></th>
<th>IgA</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Pos</td>
<td>Neg</td>
<td>Total</td>
<td>Pos</td>
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<tr>
<td>21-30</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>2</td>
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<tr>
<td>31- 40</td>
<td>8</td>
<td>8</td>
<td>16</td>
<td>3</td>
<td>13</td>
<td>16</td>
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<tr>
<td>41- 50</td>
<td>18</td>
<td>12</td>
<td>30</td>
<td>4</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>51- 60</td>
<td>22</td>
<td>14</td>
<td>36</td>
<td>4</td>
<td>32</td>
<td>36</td>
</tr>
<tr>
<td>61- 70</td>
<td>9</td>
<td>4</td>
<td>13</td>
<td>-</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>&gt;70</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Total</td>
<td>59</td>
<td>41</td>
<td>100</td>
<td>12</td>
<td>88</td>
<td>100</td>
</tr>
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**Table 2: Seroprevalence of Chlamydia genus specific antibodies in bronchial asthma group (n = 60)**

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>IgG</th>
<th></th>
<th>IgM</th>
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<th>IgA</th>
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<tbody>
<tr>
<td></td>
<td>Pos</td>
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<tr>
<td>21-30</td>
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<td>31- 40</td>
<td>11</td>
<td>4</td>
<td>15</td>
<td>3</td>
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<tr>
<td>41- 50</td>
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<td>3</td>
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<td>51- 60</td>
<td>16</td>
<td>2</td>
<td>18</td>
<td>4</td>
<td>14</td>
<td>18</td>
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<tr>
<td>61- 70</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>&gt;70</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>12</td>
<td>60</td>
<td>11</td>
<td>49</td>
<td>60</td>
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It had been postulated that acute infection with Chlamydia pneumoniae species specific IgG antibodies in asthma patients in comparison to age and sex matched controls.

Discussion

Decades ago, many clinicians believed that infection played a key role in asthma aetiology. Currently, expert opinion favours the concept that asthma is a noninfectious condition whose root cause is inflammation. Nevertheless, many unexplained aspects of asthma epidemiology, including increasing worldwide prevalence, might be related to the existence of infectious causes for asthma. Several studies attempted to associate viral or microbial infections with the occurrence or severity of asthma; however, a clear link is controversial. Reports that antibiotic treatment can improve symptoms and pulmonary function in persistent moderate and severe steroid-dependent asthma, suggest that atypical infection may be clinically relevant. In the 1990s infection with C. pneumoniae became recognized as a common aetiologic agent in community-acquired pneumonia, but also in chronic inflammatory airway diseases such as chronic obstructive pulmonary disease and asthma.[9] Chronic infection with C. pneumoniae has been documented to be common in school children and the immune response to C. pneumoniae was associated with frequency of asthma exacerbations, whereas Mycoplasma pneumoniae was not found to be important in regard to asthma exacerbation.[5] Recent infection with C. pneumoniae has also been claimed to be of importance for the development of asthma in previously healthy individuals. It had been postulated that acute C. pneumoniae infection of the respiratory tract in nonasthmatic individuals could lead to development of bronchial hyper-responsiveness. Therefore patients with a new diagnosis of asthma should be evaluated for possible C. pneumoniae infection.[5,10,11]

Several workers worldwide have shown a serological association of C. pneumoniae with chronic adult asthma.[5,12] Furthermore, population based longitudinal data from Helsinki suggest that increasing C. pneumoniae seroprevalence is associated with increasing incidence of asthma attacks in all age groups.[2] However, few studies published recently have shown no statistically significant differences in terms of prevalence of antibodies to Chlamydia pneumoniae between diagnosed asthma patients and controls.[13,14]

Our study supports an association of C. pneumoniae seroprevalence with chronic bronchial asthma. Presence of anti-chlamydia IgG antibody is indicative of chlamydial infection at an undetermined time. IgG antibodies have been shown to persist for long periods and decline very slowly. High levels of IgG antibodies are of diagnostic value in chronic/ systemic chlamydial infection provided there are no IgM antibodies.[7] We found significantly higher seroprevalence of Chlamydia genus specific IgG antibodies in patients with bronchial asthma than in similar control subjects (80% vs 59%).

Since no significant difference was found in proportion of patients positive for Chlamydia genus specific IgA and IgM antibodies in study and control group we saw no merit in evaluating all the samples for complete Chlamydia pneumoniae antibody profile. C. pneumoniae species specific IgG antibody seroprevalence was also found to be significantly high in study group in all age groups in comparison to controls (61.66% vs 38%).

The current study has several limitations. First, the number of cases recruited in study and control groups in this case control study was small. Further large prospective, cohort studies are needed to investigate the quantitative role of C. pneumoniae as an initiator of bronchial asthma.

Secondly, the high seroprevalence of C. pneumoniae antibodies in general population leaves a very narrow window for demonstrating statistically significant differences between cases and controls. However, various seroepidemiological studies done worldwide have shown a consistent association of bronchial asthma with C. pneumoniae seropositivity. The findings of the current study confirm this association in Indian population.

References

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12. Larsen FO, Norn S, Mordhorst CH, Skov PS, Milman N, Clementsen P. Chlamydia pneumoniae and possible relationship to asthma. Serum immunoglobulins and histamine release in patients and controls. APMIS 1998;106:928-34.

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