A population based seroepidemiological survey of Chlamydia pneumoniae infections in schoolchildren

G Dal Molin, B Longo, T Not, A Poli, C Campello

Aim: A serosurvey was carried out in schoolchildren from a northeastern area of Italy to define the burden of Chlamydia pneumoniae infection.

Methods: A sample of 649 schoolchildren underwent a simplified version of the International Study of Asthma and Allergies in Childhood questionnaire and IgG and IgA antibodies were investigated using an enzyme immunoassay, followed by a microimmunofluorescence assay in reactive sera.

Results: Of the children examined, 29% and 19.7% had IgG and IgA antibodies, respectively. The IgG prevalence increased with age. No other sociodemographical variable was related to C pneumoniae infection. An association was established between IgA prevalence and previous otitis media.

Conclusions: A mesoendemic (intermediate between high and low endemic level) pattern of C pneumoniae infection is present in schoolchildren from this area and the prevalence rate is related to age. Moreover, this is the first epidemiological evidence of the role of C pneumoniae in otitis.

Abbreviations: CI, confidence interval; EIA, enzyme immunoassay; MIF, microimmunofluorescence; OR, odds ratio
dilution of 1/20, and the final titre was expressed as a reciprocal. IgA was assessed by MIF only in the starting dilution and expressed as a positive or negative result.

Statistical analysis

The data are presented as frequency, geometric mean of serum titres, and median. The differences in proportions were tested with the χ² test or Fisher’s exact test, when requested by the lowest expected frequency. The linear trend was tested with Pearson’s correlation test. The differences between means were evaluated using the Student’s t test. The data were analysed using SPSS 10.0 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

The sample resulting from the cluster sampling method was compared with the reference population for age and sex (table 1), and the frequency distribution for the two variables was similar in the two groups.

Table 2 shows the seroprevalence data, according to age and sex. Overall, 29% and 19.7% of schoolchildren had antibodies belonging to the IgG and IgA classes, respectively; all IgA positive (128) children were also IgG positive.

The seroprevalence rates did not differ significantly according to sex. The prevalence rates seemed to increase with age, but the test for linear trend was not significant, probably owing to the narrow age range. However, subdividing the sample by the median (9 years), the difference in IgG prevalence was significant (25.3% in the youngest v 32.4% in the others; odds ratio (OR), 1.41; 95% confidence interval, 1.005 to 1.992; p = 0.046).

The IgG and IgA prevalence rates and the IgG geometric mean titres were compared in the two groups, because the OR was 1.6 with a 95% CI of 0.9 to 2.9 (p = 0.07). In addition, IgA prevalence seemed to appear when the prevalence of IgG was substantially higher in children with previous otitis, albeit in a non-significant way. Nevertheless, a trend towards significance seemed to appear when the prevalence of IgG was compared in the two groups, because the OR was 1.81 with a 95% CI of 0.9 to 3.37 (p = 0.05). In table 3, the positivity of *C pneumoniae* antibodies is analysed in relation to certain respiratory disorders.

<table>
<thead>
<tr>
<th>Variable (N)</th>
<th>IgG positive</th>
<th>IgA positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys (358)</td>
<td>102</td>
<td>28.5</td>
</tr>
<tr>
<td>Females (291)</td>
<td>86</td>
<td>29.6</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 (69)</td>
<td>16</td>
<td>22.2</td>
</tr>
<tr>
<td>7 (119)</td>
<td>29</td>
<td>24.4</td>
</tr>
<tr>
<td>8 (111)</td>
<td>30</td>
<td>27.0</td>
</tr>
<tr>
<td>9 (116)</td>
<td>44</td>
<td>37.9</td>
</tr>
<tr>
<td>10 (118)</td>
<td>36</td>
<td>30.5</td>
</tr>
<tr>
<td>&gt;11 (116)</td>
<td>33</td>
<td>28.4</td>
</tr>
<tr>
<td>Total</td>
<td>649</td>
<td>29.0</td>
</tr>
</tbody>
</table>

Neither breast feeding, nor a family history of allergy correlated with the *C pneumoniae* immune response. Day nursery attendance (children from 6 months to 2 years) did not seem to affect the prevalence; kindergarten attendance (children 3–5 years) was not investigated because almost all children had this exposure. The environmental factors explored—external tobacco smoke and number of siblings—did not correlate with *C pneumoniae* antibodies. With regard to external tobacco smoke, IgG and IgA reactivity was higher in exposed children, but the relation was not significant. Social conditions, evaluated by the parents’ schooling level, were not significantly associated with *C pneumoniae* infection.

In table 3, the positivity of *C pneumoniae* antibodies is analysed in relation to certain respiratory disorders.

<table>
<thead>
<tr>
<th>Variable (N)</th>
<th>IgG positive</th>
<th>IgA positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis/conjunctivitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (53)</td>
<td>19</td>
<td>35.8</td>
</tr>
<tr>
<td>No (596)</td>
<td>169</td>
<td>28.4</td>
</tr>
<tr>
<td>Sinusitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (18)</td>
<td>5</td>
<td>27.8</td>
</tr>
<tr>
<td>No (631)</td>
<td>183</td>
<td>29.0</td>
</tr>
<tr>
<td>Orsitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (54)</td>
<td>20</td>
<td>37.0</td>
</tr>
<tr>
<td>No (595)</td>
<td>168</td>
<td>28.2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (7)</td>
<td>1</td>
<td>14.3</td>
</tr>
<tr>
<td>No (642)</td>
<td>187</td>
<td>29.1</td>
</tr>
<tr>
<td>Hospitalisation for asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (12)</td>
<td>1</td>
<td>8.3</td>
</tr>
<tr>
<td>No (637)</td>
<td>187</td>
<td>29.4</td>
</tr>
<tr>
<td>Ever asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (47)</td>
<td>8</td>
<td>17.0</td>
</tr>
<tr>
<td>No (602)</td>
<td>180</td>
<td>29.9</td>
</tr>
</tbody>
</table>

*Odds ratio, 1.81; 95% confidence interval, 1.00 to 3.37; p = 0.05. GM, geometric mean of IgG titres.
DISCUSSION
This is one of the largest population-based, cross-sectional surveys performed to date on the prevalence of *C. pneumoniae* in children. About 7.5% of the reference population living in an urban area of northeastern Italy was screened for *C. pneumoniae* antibodies. We believe that the sampling method, coupled with the very low refusal rate among eligible subjects, led to the enrolment of an unbiased group of children. Overall, 29% of the studied subjects tested positive for *C. pneumoniae* IgG antibodies. Therefore, the pattern of *C. pneumoniae* infection in this area may be defined as mesoendemic, intermediate between the low prevalence rates recorded in North America and northern Europe, but substantially lower than those reported in series from Taiwan, Japan, Spain and in general from tropical areas.\(^2\) \(^1\) \(^{11} \) \(^{17}\) In addition, our data agree with two previous reports from Italy.\(^1\) \(^8\) \(^9\)

"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"\(^1\)

The reasons for these wide geographical differences are poorly understood. It has been claimed that seroprevalence rates are related to population density\(^2\); however, crowding and hygienic conditions could be more relevant. In this respect, our study revealed no clear exposure (or protective factor) that could be related to *C. pneumoniae* antibody prevalence, except for age. An increase in seroprevalence was evident when comparing the groups under and over the median, thus underlining the importance of school settings in favouring *C. pneumoniae* transmission. Nevertheless, an IgG antibody prevalence rate of about 23% in the first age class is consistent with an early exposure to *C. pneumoniae* infection in the community.\(^7\) \(^8\) We found that the seroprevalence was not related to crèche attendance, family crowding, social status, or external tobacco smoke. Collectively, our data show that several social and environmental conditions are not related to the burden of *C. pneumoniae* infection in this area, and that only strong differences in exposure could translate into substantial differences in seroprevalence.

The role of *C. pneumoniae* in child pneumonia has been well established in prospective studies carried out in clinical settings, although variation in rates, ranging from a few cases to 10%, were reported.\(^1\) \(^2\) \(^3\) \(^10\) \(^10\) \(^19\) \(^19\) In this population-based study, the rarity of this disease made the association impossible to assess.

The role of *C. pneumoniae* in asthma is still debatable, at least in some groups of patients. According to our study, primary infections occurring in children may not be important for asthma onset, although in adults *C. pneumoniae* infections can act as a trigger for an already existing disorder.\(^2\) \(^6\) \(^8\) \(^9\) \(^10\) \(^24\) \(^26\) \(^28\)

The role of *C. pneumoniae* infection in otitis media (acute otitis media or secretory otitis media) has been defined in recent years. The presence of *C. pneumoniae* in fluid from the middle ear was repeatedly confirmed, in spite of a single large series with negative results (D Davis *et al.* Failure to detect *Chlamydia pneumoniae* in middle ear aspirates from patients with otitis media with effusion [abstract]. Proceedings of the 97th general meeting of the American Society for Microbiology, Miami Beach, Florida, USA, 4–8 May 1997:C-351).\(^2\) \(^20\) \(^26\) \(^29\) The involvement of *C. pneumoniae* in middle ear flogosis has been confirmed by our survey. IgG prevalence and a high IgG titre, expressed as a geometric mean, showed a trend in significance for the outcome, namely otitis media occurring in the past year. Moreover, we found a significant relation between IgA seroprevalence and otitis. IgA reactivity, alone or coupled with high IgG titres, was frequently considered to be an indirect marker of chronic or persistent *C. pneumoniae* infection, because of the short half-life of this class of immunoglobulin. In our survey, the distinction between acute otitis and chronic/recurrent otitis could not be made: this issue needs to be studied further. Nevertheless, *C. pneumoniae* seems to play a role in otitis media. Therefore, this aetiology must be considered in the clinical setting whenever evidence of the most common pathogens is lacking; furthermore, *C. pneumoniae* should be suspected as a possible co-pathogen when treatment with a β-lactamic proves unsuccessful.

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REFERENCES


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