**Original Article**

Rarity of Bacterial and Viral Meningitis in Areas of Western Greece with Fewer than 2,000 Inhabitants

Giannakopoulos Ioannis, Leotsinidis Michael*, Diamantopoulos Stavros, Makrakis Konstantinos, Ellina Aikaterini, Giannakopoulos Ageilos and Papanastasiou Dimitris, A*

Department of Pediatrics, School of Medicine, University of Patras, and Laboratory of Public Health, School of Medicine, University of Patras, and Department of Health of Western Greece, Patras, Greece

(Received February 19, 2007. Accepted November 19, 2007)

**SUMMARY:** The purpose of the present study was to compare the incidence of childhood meningitis in regions with fewer than 2,000 inhabitants (rural regions) and regions with more than 2,000 inhabitants (urban regions) in the prefecture of Achaia in Western Greece during 1991 - 2005. Included were all 555 children hospitalized for meningitis. The criteria for bacterial meningitis were (i) positive blood/cerebrospinal fluid (CSF) culture, Gram stain, or latex agglutination and/or (ii) increased \( \beta \)-glucuronidase in CSF. In case of suspected bacterial meningitis, the following findings were considered: compatible clinical and laboratory findings, and whether or not a cure was achieved with antibiotic treatment and finally resulted in negative cultures. In cases of suspected viral meningitis, compatible clinical and laboratory findings were considered, together with observation of a cure without antibiotic treatment. Only 28 of 555 meningitis patients were from rural regions. The incidence per 10,000 children in rural and urban regions, respectively, was as follows: meningitis, 1.13 and 8.99; bacterial meningitis, 0.16 and 2.40; suspected bacterial meningitis, 0.52 and 3.00; and viral meningitis, 0.44 and 3.58. The incidence ratio for bacterial, suspected bacterial, and viral meningitis in urban versus rural regions was 14.85, 5.72, and 8.10, respectively. Only 2 of the 79 cases with a confirmed causative pathogen came from rural regions. In conclusion, compared to those living in urban regions, children living in rural regions are relatively spared from bacterial and viral meningitis.

**INTRODUCTION**

Meningitis is a major cause of morbidity and mortality throughout the world. Many studies have investigated possible risk factors for developing bacterial or viral meningitis. Factors implicated in meningococcal meningitis include overcrowding (1-3), social gathering (4), smoking (5), low socioeconomic status, and young age (6). Day-care attendance, early exposure to other children, and young age have been associated with pneumococcal (7) and hemophilus meningitis (8). Children at high risk for pneumococcal disease are those with asplenia, sickle cell disease and nephrotic syndrome, HIV and other immunodeficiencies, and cerebrospinal fluid (CSF) leaks (9). As regards viral meningitis, enteroviruses are the major pathogens (85-90%), and risk factors for children include young age, poor hygiene practices (hand washing), and day-care or playground attendance (10,11).

Many infections in childhood are acquired from close contact between daycare or school peers. In our population, classrooms in urban areas were notably more crowded (19.3 students/classroom) than those in rural areas (10.4 students/classroom). Furthermore, it is common practice for young children living in rural areas of Greece to be supervised by an elderly member of the family or by mothers.

An increased incidence of meningitis in urban compared to rural populations has been reported in studies from Cordoba (12), Tennessee (13), and more recently, England (14). However, no specific definition of rural versus urban areas is provided any of these studies.

The present study was conducted in order to investigate possible differences between urban and rural settings in terms of the incidence of bacterial and viral meningitis.

**MATERIALS AND METHODS**

This descriptive study includes all children affected by meningitis in Achaia County of Western Greece during the years 1991 to 2005 who were treated in the two regional hospitals for children. All children with meningitis in this county were treated at one of these two hospitals. The medical files of all patients were available for retrospective evaluation of the data.

Bacterial meningitis was diagnosed in children with compatible signs and symptoms of bacterial meningitis, i.e., pleocytosis in the CSF with an additional positive culture, and/or positive Gram stain and/or latex agglutination and/or increased \( \beta \)-glucuronidase in the CSF (15). In addition, children with signs and symptoms of meningitis, pleocytosis in the CSF, and a positive blood culture were considered to have bacterial meningitis based on the isolated pathogen. Thus, patients with bacterial meningitis were divided in two categories: (i) those with a confirmed bacterial pathogen and (ii) those without a confirmed bacterial pathogen but with increased \( \beta \)-glucuronidase in the CSF.

Diagnosis of suspected bacterial meningitis included signs and symptoms of meningitis treated with antibiotics before admission, but with negative blood or CSF cultures, a negative Gram stain, and a negative latex agglutination test. All patients in this category had laboratory findings (leukocyte count, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP] and cells, protein, and glucose in the CSF) compatible with a bacterial infection. In these patients, no
CSF β-glucuronidase measurements were not performed. Patients lacking previous treatment with antibiotics, but with clinical and laboratory findings compatible with viral meningitis and with negative blood or CSF cultures, with a negative Gram stain and a negative latex agglutination test, and those lacking increased β-glucuronidase in the CSF were considered to have viral meningitis. No specific tests for virus identification were carried out in most of these cases.

The prefecture of Achaia (Western Greece) in which the study was performed is geographically and demographically well defined. According to the census registration, the average population of the region for the study period of 1991 - 2005 consisted of 311,435 people. Of these individuals, 58,071 (18.64%) were 14 years old or younger (30,092 males and 27,979 females).

According to the categorization of the Ministry of the Interior, urban areas are defined as those with more than 2,000 inhabitants, while those with less than 2,000 inhabitants are considered as rural areas. In the prefecture of Achaia, there are five urban areas with a total population of 208,538 people, while the remainder (102,897 people) live in rural areas (census 2001). Therefore, all residents and meningitis patients were divided into two groups according to whether they were inhabitants of urban or rural areas. The number of children living in an urban region was 40,961 (70.5%) and that of children living in a rural region was 17,110 (29.5%). According to data from the National Statistics Service, the mean population density in rural and urban areas of Achaia was 24.8 and 388.7 residents/km², respectively.

The total incidence of meningitis and that of subgroups with the disease, as defined above, were compared in the two regions.

Statistical analysis was conducted using the SPSS release 13.0 statistical package (SPSS, Inc., Chicago, Ill., USA). Poisson regression was applied to estimate the incidence rate between the areas (16).

**RESULTS**

There were 555 children with documented bacterial, suspected bacterial, or viral meningitis. The patients were 14 years old or younger, but older than 1 month.

The total meningitis incidence plotted over time for the 15-year period of the study is presented in Figure 1. There was an increase in the incidence of meningitis in the years 1997, 1998, 1999, 2000, 2001, and 2002 in the populations inhabiting urban regions, and an increase was also observed in rural regions in the years 2001 and 2002. This increase involved primarily children up to 4 years of age during the entire study period, except for in the year 2001, as depicted in Figure 2. During the year 2001, children aged 5-9 years were predominantly affected.

The number of children with bacterial, suspected bacterial, or viral meningitis and the corresponding incidences in urban and rural regions of Achaia are shown in Table 1. Only 28 of 555 meningitis patients were from a rural region, 4 of these had bacterial meningitis, 11 viral, and 13 suspected bacterial meningitis. The incidence of meningitis in the rural regions was 8 times lower than that in urban regions. Table 1 shows the total number of meningitis cases as well as the incidence of meningitis stratified by different age groups. For all age groups, bacterial, suspected bacterial, and viral meningitis were more prevalent and their incidences higher in urban areas than in rural areas. The incidence rate between regions are presented in Table 2. The incidence rate of meningitis for the urban and rural regions were significantly different, not only in the case of bacterial meningitis, but also for viral and suspected bacterial meningitis.

The pathogens isolated were *Haemophilus influenzae* type b, *Neisseria meningitidis*, and *Staphylococcus pneumoniae*. Table 3 shows the number of children with bacterial meningitis due to *H. influenzae* type b, *N. meningitidis*, *S. pneumoniae* and that of children with bacterial meningitis diagnosed by
Similar results were reported in the pre-meningitis. A study in Cordoba found a greater incidence of urban and rural populations in terms of the incidence of meningococcal and vaccination era from a study carried out in Tennessee (USA), where cases of meningococcal and H. influenzae type b meningitis were significantly more frequently observed in urban than in the rural area studied. In contrast to other studies, our focus was on children, and the time frame covered an extended period, which allowed for the comparison of annual incidences between areas. As shown in Figure 1, the incidence of meningitis in the rural regions was lower than that in the urban areas studied here.

It would be reasonable to suspect the impact of various risk factors for bacterial (1-8) and viral (10,11) meningitis (e.g., overcrowding, smoking, social gathering, low socioeconomic status, previous viral illness, day-care attendance) differ in urban and rural regions, with associated differences in the incidence of meningitis in these regions. Since children 4 years old and younger were primarily affected throughout the 15-year period, with the exception of the year 2001 (Fig. 2), it is clear that of particular importance are any differences in risk factors in rural and urban areas related principally to this age group.

For young children, daycare centers are typical sites for exposure to and acquisition of upper respiratory tract viral infections (17). Daycare centers in general, and healthcare practices at such centers in particular, have been found to play a role in small outbreaks of viral meningitis (10), a disease caused mainly by non-polio enteroviruses (11). In many rural areas of our study, there were no daycare centers, although it should be noted that data were not available for all areas included in the study.

Furthermore, there was a higher proportion of elderly inhabitants in the rural areas, a factor that might have played a role in transmission; additionally in rural areas, there was a corresponding decreased proportion of young adults, a group that has been suggested to have the highest meningococcus carriage rates in non-rural regions (11).

The striking difference in the incidence of meningitis among children living in rural and urban areas might represent a combination of the aforementioned factors. However, the existence of a single determinative factor protective against meningitis in children living in rural regions cannot be excluded.

The large number of cases of suspected bacterial meningitis hindered arriving at accurate conclusions regarding specific pathogens. Moreover, a substantial number of cases characterized as “suspected bacterial” meningitis were probably viral meningitides. However, this possibility would not affect the present results, because documented viral as well as documented bacterial meningitis have similar incidences in rural or urban regions.

The validity of our study might have suffered from under-reporting: however, all meningitis cases in our district were bound to receive medical attention at one of the two pediatric hospitals of the area, and all were reported to the Regional Department of Health. Therefore all meningitis cases, especially bacterial cases, would have received medical care and would have been included in the present study. One remaining question would be whether all patients with viral meningitis received an accurate diagnosis and were therefore admitted to one of the two hospitals and subsequently reported to the Regional Department of Health. However, a misdiagnosis would not have greatly affected the results, because whether or not a diagnosis of viral meningitis was made was a random event.

In conclusion, differences in the incidence of bacterial meningitis between urban and rural populations have been described here and in previous studies. However, explanations for these differences remain incomplete. The strikingly low incidence of meningitis observed in rural regions relative to

### Table 2. Incidence ratio of meningitis between urban and rural regions

<table>
<thead>
<tr>
<th>Type of meningitis</th>
<th>Incidence ratio①</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected bacterial</td>
<td>5.72</td>
<td>3.26</td>
</tr>
<tr>
<td>Viral</td>
<td>8.10</td>
<td>4.42</td>
</tr>
<tr>
<td>Bacterial</td>
<td>14.85</td>
<td>5.50</td>
</tr>
<tr>
<td>Total</td>
<td>7.96</td>
<td>5.44</td>
</tr>
</tbody>
</table>

①: Poison regression.

### Table 3. Cases of bacterial meningitis in prefecture of Achaia

<table>
<thead>
<tr>
<th>Type of bacterial meningitis</th>
<th>Urban</th>
<th>Rural</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. influenzae type b</td>
<td>17</td>
<td>0</td>
<td>17.00</td>
</tr>
<tr>
<td>N. meningitidis</td>
<td>54</td>
<td>0</td>
<td>56.00</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>6</td>
<td>0</td>
<td>6.00</td>
</tr>
<tr>
<td>Proven by increased β-glucuronidase</td>
<td>64</td>
<td>0</td>
<td>64.00</td>
</tr>
</tbody>
</table>

### Table 4. Incidence ratio of bacterial meningitis between areas

<table>
<thead>
<tr>
<th>Area</th>
<th>Type of meningitis</th>
<th>Incidence ratio①</th>
<th>Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban versus Rural</td>
<td>H. influenzae type b</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td></td>
<td>N. meningitidis</td>
<td>11.36</td>
<td>2.77</td>
</tr>
<tr>
<td></td>
<td>S. pneumoniae</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td></td>
<td>Proven by increased β-glucuronidase</td>
<td>13.50</td>
<td>3.30</td>
</tr>
</tbody>
</table>

①: Poison regression.

†: There were no cases either in one area or in the other one or even in both of them.

increased β-glucuronidase in the CSF living in urban or rural regions. Of the 145 bacterial meningitis cases, only 4 (i.e., 2 with meningococcal meningitis and 2 detected by increased β-glucuronidase) came from a rural region. Patients with meningitis due to H. influenzae type b and S. pneumoniae came exclusively from urban regions. The incidence rate between areas for the various types of bacterial meningitis are presented in Table 4. The incidence rate between the rural versus the urban regions was 11.36 for meningitis due to N. meningitidis and 13.50 for bacterial meningitis confirmed by increased β-glucuronidase in the CSF. Calculations for meningitis due to H. influenzae type b and S. pneumoniae could not be carried out, because no such case of meningitis occurred in rural regions.

**DISCUSSION**

There have been previous reports of differences between urban and rural populations in terms of the incidence of meningitis. A study in Cordoba found a greater incidence of bacterial meningitis in the city compared to the province (12). Similar results were reported in the pre-H. influenzae type b vaccination era from a study carried out in Tennessee (USA), where cases of meningococcal and H. influenzae type b meningitis were significantly more frequently observed in urban than in rural populations. Pneumococcal meningitis was also more frequently observed, but the results did not reach statistical significance (13). A recent retrospective study (14) performed in England revealed that the average annual incidence of meningococcal disease was higher in the urban area
that in urban regions should be investigated in future studies in order to document potential factors that are protective against contracting meningitis in these settings.

REFERENCES