# High incidence of childhood pneumonia at high altitudes in Pakistan: a longitudinal cohort study

Aamir J Khan,<sup>a</sup> Hamidah Hussain,<sup>a</sup> Saad B Omer,<sup>a</sup> Sajida Chaudry,<sup>b</sup> Sajid Ali,<sup>c</sup> Adil Khan,<sup>d</sup> Zayed Yasin,<sup>d</sup> Imran J Khan,<sup>d</sup> Rozina Mistry,<sup>e</sup> Imam Yar Baig,<sup>e</sup> Franklin White,<sup>c</sup> Lawrence H Moulton<sup>a</sup> & Neal A Halsey<sup>a</sup>

**Objective** To determine the incidence of pneumonia and severe pneumonia among children living at high altitudes in Pakistan. **Methods** A longitudinal cohort study was conducted in which 99 female government health workers in Punial and Ishkoman valleys (Ghizer district, Northern Areas of Pakistan) enrolled children at home, conducted home visits every 2 weeks and actively referred sick children to 15 health centres. Health centre staff used Integrated Management of Childhood Illness criteria to screen all sick children aged 2–35 months and identify those with pneumonia or severe pneumonia.

**Findings** Community health workers enrolled 5204 eligible children at home and followed them over a 14-month period, ending on 31 December 2002. Health centre staff identified 1397 cases of pneumonia and 377 of severe pneumonia in enrolled children aged 2–35 months. Among children reported with pneumonia, 28% had multiple episodes. Incidence rates per 100 child-years of observation were 29.9 for pneumonia and 8.1 for severe pneumonia. Factors associated with a high incidence of pneumonia were younger age, male gender and living at high altitude.

**Conclusion** Pneumonia incidence rates in the Northern Areas of Pakistan are much higher than rates reported at lower altitudes in the country and are similar to those in high-altitude settings in other developing countries. More studies are needed to determine the causes of pneumonia in these high-mountain communities. However, early introduction of the vaccines that are known to prevent pneumonia should be considered.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

# Introduction

Pneumonia is a leading cause of childhood death in countries with high mortality rates among children under 5 years of age, and it continues to be the second leading cause of death among such children in Pakistan.<sup>1,2</sup> In Abbottabad, in the north-western part of Pakistan, the cause-specific mortality rate from pneumonia in children under 5 years of age was reported to be 14 deaths per 1000 children annually before interventions.<sup>3</sup> In a village at approximately 1525 m above sea level in the Northern Areas of Pakistan, 44% of all deaths in children under 5 years of age between 1988 and 1991 were due to pneumonia, based on verbal autopsy methods.<sup>4</sup> Surveillance of mortality by the Aga Khan Health Services, Pakistan (AKHSP) in the Northern Areas, based on verbal autopsy, indicated that pneumonia continues to cause approximately 33% of deaths in infants and 37% of deaths in children aged 1–4 years.<sup>5</sup>

Pneumonia incidence is most strongly and consistently associated with young age, with the highest reported rates in children aged 2–6 months.<sup>6,7</sup> Rudan et al. suggest that, worldwide, most episodes (> 95%) of early childhood pneumonia in children aged 0–4 years occur in developing countries, at an incidence rate of 0.28 episodes per year.<sup>8</sup> The high incidence of pneumonia in infants and children living at high altitudes is well established from studies in the Peruvian Andes and Papua

New Guinea, with rates of 30 episodes per 100 child-years of observation and higher.<sup>9,10</sup> Other factors associated with pneumonia include male gender,<sup>7</sup> malnutrition,<sup>11,12</sup> micronutrient deficiency,<sup>13,14</sup> low immunization coverage,<sup>15,16</sup> low household income,<sup>17</sup> overcrowding,<sup>18</sup> poor breastfeeding practices<sup>19,20</sup> and exposure to indoor air pollution.<sup>21,22</sup>

In 1984, a cohort study of 1476 infants in Lahore reported a pneumonia incidence rate of 22 per 100 child-years of observation.<sup>23</sup> The study had limitations – diagnoses were based on maternal recall, recurring symptoms were reported as a single episode, and there was no concurrent facility-based surveillance system.<sup>24,25</sup> In 2002, a study of children aged 2–59 months in Karachi found low pneumonia rates (8.2 per 100 child-years of observation), but the study was limited by the small proportion of cases that presented at study clinics.<sup>26</sup> Unpublished studies conducted near Gilgit (capital of the Northern Areas of Pakistan) during the 1990s found an incidence of 30 cases of pneumonia per 100 child-years of observation in children under 5 years of age.<sup>27</sup>

The purpose of this study was to determine the incidence of pneumonia and severe pneumonia by age and altitude in a cohort of children living at high altitudes in the Himalayan regions of Pakistan, followed from 2 to 35 months of age.

<sup>&</sup>lt;sup>a</sup> Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States of America (USA).

<sup>&</sup>lt;sup>b</sup> Preventive Medicine Residency Program, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA.

<sup>°</sup> Community Health Sciences Department, Aga Khan University, Karachi, Pakistan.

<sup>&</sup>lt;sup>d</sup> Center for Health Interventions Research, Gilgit, Pakistan.

<sup>&</sup>lt;sup>e</sup> Aga Khan Health Services, Pakistan, Karachi, Pakistan.

Correspondence to Aamir J Khan (e-mail: ajkhan@jhsph.edu).

<sup>(</sup>Submitted: 10 October 2007– Revised version received: 1 July 2008 – Accepted: 2 July 2008 – Published online: 29 January 2009)

 Table 1. Incidence of pneumonia and severe pneumonia among children 2–35 months of age, by altitude, Punial and Ishkoman valleys, Pakistan, 1 September 2001 to 31 December 2002

| Altitude<br>range, in<br>metres | Characteristics of enrolled children          |                       |   |  | All health facilities under surveillance |   |  |                                       |
|---------------------------------|---|-----------------------|---|--|--|---|--|---------------------------------------|
|                                 | Children<br>enrolled,<br>No. (%) <sup>a</sup> | CYO, in<br>years (%)ª | Pneumonia<br>incidence,<br>per 100 CYO <sup>b</sup> | Severe pneumonia<br>incidence,<br>per 100 CYO <sup>b</sup> | Health<br>centres,<br>No.°               | Pneumonia<br>cases,<br>No. (%) <sup>d</sup> | Severe pneu-<br>monia cases,<br>No. (%) <sup>d</sup> | All pneumo-<br>nia cases,<br>No. (%)° |
| 1675-1980                       | 2656 (51)                                     | 2599 (54)             | 20  | 8.7  | 8  | 702 (75)                                    | 229 (25)   | 931 (53)                              |
| 1980-2285                       | 1511 (29)                                     | 1384 (29)             | 40.2  | 8.5  | 4  | 530 (84)                                    | 102 (16)   | 632 (36)                              |
| 2286-2590                       | 817 (16)                                      | 706 (15)              | 30.5  | 11   | 5  | 165 (82)                                    | 37 (18)  | 202 (11)                              |
| > 2590                          | 220 (4)                                       | 160 (3)               | NA <sup>f</sup>                                     | 18.4   | 2  | 0   | 9 (100)  | 9 (< 1)                               |
| All altitudes                   | 5204 (100)                                    | 4849 (100)            | 29.9  | 8.1  | 19                                       | 1397 (79)                                   | 377 (21)   | 1774 (100)                            |

CYO, child-years of observation; NA, not applicable.

<sup>a</sup> Per cent of all children enrolled at home.

<sup>b</sup> Child-years of observation based on data between 1 November 2001 and 31 December 2002.

<sup>c</sup> Surveillance was stopped at four health centres due to prolonged staff absenteeism or extremely low patient volumes.

<sup>d</sup> Per cent of pneumonia or severe pneumonia cases seen at all facilities under surveillance.

<sup>e</sup> Per cent of all pneumonia cases seen at all facilities under surveillance.

<sup>f</sup> No pneumonia cases reported at this altitude range.

# **Methods**

### Setting

The Punial and Ishkoman valleys are located in the Ghizer district, north-west of Gilgit town. A paved road connects Punial to Gilgit (about 2 hours' drive), but in 2002 Ishkoman was more distant (about 6 hours' drive) and isolated, without roads. In 2001, the valleys had a combined estimated population of 59 000.28 Villages in Punial are situated at an altitude of 1675-1980 m and in Ishkoman mainly at 1980-2590 m, although two villages in Ishkoman are higher than this. The temperature ranges from -15°C to 40°C. Households commonly include more than one generation of married couples and their children. Indoor wood fires are usually used for cooking and heating. Farming is the primary means of livelihood, although younger men are likely to seek a career in the military or the government.

During 2001 and 2002, the AKHSP had 5 primary health-care centres and 1 secondary health-care centre covering Punial and Ishkoman. The government health system in Punial and Ishkoman was more extensive, with 9 primary centres and 2 secondary centres. All secondary centres and 4 primary health care centres were staffed by physicians and paramedics. In AKHSP centres, cost-recovery is considered essential for sustainability, whereas government centres charge only a nominal fee.

Since the inception of the AKHSP Primary Health Care Program, infant

mortality rates have fallen below 40 per 1000 live births. In 2000, 84% of children were fully immunized - bacille Calmette-Guérin; polio; diphtheriapertussis-tetanus; and measles - by 1 year of age, and more than 60% of infants were exclusively breastfed until 4 months of age.<sup>28</sup> However, 22% of infants and 24% of children aged 1-4 years had grade-1 malnutrition. The government-run National Health Worker Program enlists village-based, female health workers to make monthly household visits and provide primary care services at home. These health workers are trained to screen children for serious illness that requires referral and to treat simple illnesses according to WHO guidelines, including those for acute respiratory infections. The use of WHO Integrated Management of Childhood Illness (IMCI) guidelines by health workers was not part of the government programme during the study period but, for the purposes of this study, the workers were trained in the recognition and referral of IMCIclassified diseases.

## Study design and outcomes

This was a longitudinal cohort study. Initially, all children aged 2–24 months in the study area were eligible for enrolment; subsequently, all neonates were eligible for enrolment until the end of the study period. Health workers were given a financial incentive to follow children through two home visits per month (normally only one is scheduled). They screened children for IMCI signs of cough or difficulty breathing and measured respiratory rates, both during home visits and whenever sick children were brought to the health worker's home. All children with IMCIclassified general danger signs, pneumonia or severe pneumonia were referred to the closest health centre. IMCI general danger signs include lethargy or unconsciousness, convulsions, inability to drink or breastfeed, and vomiting everything. Pneumonia was defined as a history of cough or difficulty breathing plus fast breathing (respiratory rates above IMCI cut-off points for age) on observation; severe pneumonia was defined as cough or difficulty breathing plus any general danger sign or chest in-drawing or stridor.29

Health workers are provided with co-trimoxazole under the government programme, but it was often unavailable for months and was usually reserved for severely ill children. Even when treatment was provided, health workers were asked to refer all suspected pneumonia and severe pneumonia cases to health centres. Health-centre staff screened all sick children and identified those with pneumonia or severe pneumonia (the primary outcomes) as defined under the IMCI guidelines for children aged 2 months to 5 years.<sup>29</sup> Children under 2 months were not included in this analysis because IMCI guidelines do not have a separate classification for pneumonia or severe pneumonia for these young infants; instead, they group all serious illness in such infants as possible serious bacterial infection.

# **Eligibility and enrolment**

Children under 24 months of age living in Punial or Ishkoman were eligible and were enrolled at their homes between 24 July 2001 and 31 October 2001. All neonates were eligible, and enrolment took place between 24 July 2001 and 31 December 2002. Enrolled children were given a unique identification number using a code based on the area, health worker, household and mother. Each mother was given an identification card and asked to present it when visiting the health centre with her sick child.

## **Home visits**

Enrolled children were visited at home every 2 weeks by the health workers, who recorded whether the child was alive and present, signs and symptoms of current illness, symptoms of past illness (based on the care provider's 2-week recall) and immunizations received.

# Identification of sick children at health centres

For this study, health-centre staff screened all children aged 2-35 months and identified all cases of pneumonia and severe pneumonia. Surveillance for IMCI-classified pneumonia and severe pneumonia among children aged 2-35 months was phased in across health centres over a 2-month period starting from 1 September 2001. The 19 health centres participating in the study included 12 government primary health-care centres, 5 AKHSP primary health-care centres, a commercially run private clinic and a charity-sponsored clinic. Surveillance was stopped at 4 centres (3 government first aid posts and the private clinic) in December 2001 due to staff leave of absence or low patient turnout. The exclusion of these centres was considered justified because these areas were served by other accessible, more heavily trafficked health centres, and would not affect case recognition or management. Surveillance at 15 health centres continued until 31 December 2002.

### **IMCI training**

During the study, 99 female health workers, 11 programme supervisors, 8 medical officers and 17 paramedical staff in the government health system were trained and evaluated in the use Table 2. Characteristics of 1260 children aged 2–35 months with pneumonia and<br/>severe pneumonia seen at first-level health facilities, Punial and Ishkoman<br/>valleys, Pakistan, 1 September 2001 to 31 December 2002

| Characteristics                            | Pneumonia cases<br>( <i>n</i> = 1397) | Severe pneumonia cases<br>(n = 377) |
|--|---------------------------------------|-------------------------------------|
| Parental history, No. (% or SD)            |                                       |                                     |
| Mother is information provider             | 1256 (90)                             | 337 (89)                            |
| Mean age of children in months             | 12.1 (7.8)                            | 11.7 (7.5)                          |
| Child is male                              | 757 (54)                              | 201 (53)                            |
| Antibiotic received before current visit   | 110 (8)                               | 80 (21)                             |
| Co-trimoxazole                             | 55 (4)                                | 34 (9)                              |
| Amoxicillin                                | 46 (3)                                | 34 (9)                              |
| Others                                     | 4 (< 1)                               | 4 (< 1)                             |
| Child is able to breastfeed or drink       | 1396 (100)                            | 331 (88)                            |
| Child vomits everything                    | 0                                     | 79 (21)                             |
| Mean number of days                        | NA                                    | 2.1 (1.8)                           |
| Child had convulsions                      | 0                                     | 33 (9)                              |
| Mean number of days                        | NA                                    | 2.9 (1.7)                           |
| Child has a cough                          | 1380 (99)                             | 366 (97)                            |
| Mean number of days                        | 2.9 (2.5)                             | 3.3 (2.8)                           |
| Child has difficulty breathing             | 466 (33)                              | 263 (70)                            |
| Mean number of days                        | 2.4 (3.0)                             | 2.3 (1.7)                           |
| Child has a fever                          | 1358 (97)                             | 350 (93)                            |
| Mean number of days                        | 2.6 (1.4)                             | 3.4 (6.1)                           |
| If fever for $> 7$ days, present every day | 9 (< 1)                               | 11 (3)                              |
| Child has diarrhoea                        | 66 (5)                                | 35 (9)                              |
| Mean number of days                        | 3.9 (7.2)                             | 5 (3.8)                             |
| Observation, No. (%)                       |                                       |                                     |
| Lethargic or unconscious                   | 0                                     | 30 (8)                              |
| Febrile (> 37.5 °C)                        | 572 (41)                              | 193 (51)                            |
| Fast breathing                             | 1397 (100)                            | 368 (98)                            |
| Chest in-drawing                           | 0                                     | 262 (69)                            |
| Stridor                                    | 0                                     | 144 (38)                            |

NA, not applicable; SD, standard deviation.

of IMCI guidelines.<sup>29</sup> Refresher training was given to 3 medical officers and 8 female paramedics at AKHSP facilities previously trained in the use of IMCI guidelines. For health-centre staff, particular emphasis was placed on the recognition and management of pneumonia, and the recognition and referral of severe pneumonia. All community and facility-based staff were visited by project supervisors every 2 weeks to review home-visit schedules, data forms, IMCI classification of disease and referral practices. All IMCI classifications on data forms were checked for internal consistency against the signs, symptoms and physical examination findings recorded. Health workers were offered intensive follow-up training every 6 weeks during the course of the study. The impact of this training is covered in a separate paper, where we conclude that it led to sustained

improvements in performance, disease recognition and referral during the course of surveillance.

#### Statistical methods

The age-specific incidence of pneumonia and severe pneumonia was calculated by dividing the total number of cases identified at all participating health facilities by the months of observation contributed by children. Incidence rate calculations were based on the outcomes detected from 1 November 2001 (when the baseline home-based enrolment had been completed) to 31 December 2002. Associations between the incidence of disease and age, altitude and number of other children in the household were explored using Poisson regression analysis.

The records of sick children enrolled at health centres were verified, and only those cases meeting IMCI criteria were included in the analysis. The months of observation contributed by individual children were calculated from the date of enrolment to the date the child reached the age of 36 months, was reported to have died or had migrated out of the surveillance area. To account for children who moved out of the surveillance area temporarily (including accompanying the mother to summer-time pastures) we subtracted the weeks of observation the child was reported not to have been at home on three or more consecutive visits.

Information collected at the time of home-based enrolment and on subsequent home visits was linked with the information collected at participating health facilities. If the child's surveillance number was unavailable, we could procure it at a later date based on additional information collected at the time of the facility visit.

Forms used at the site were optimized for scanning and optical character recognition using TELEform<sup>®</sup> 6 (Cardiff Software Inc., Sunnyvale, CA, United States of America) and data integrity was checked using Microsoft Access<sup>®</sup> 2000 (Microsoft Corporation, Seattle, WA, USA). Data were analysed using SPSS<sup>®</sup> version 11.5 (SPSS Inc., Chicago, IL, USA) for frequency analysis and cross-tabulation, and STATA<sup>®</sup> version 8.0 (College Station, TX, USA) for regression analysis.

# Institutional review board approvals

This study was approved by the institutional review boards at the Johns Hopkins Bloomberg School of Public Health and the Aga Khan University. Written informed consent from parents or legal guardians was obtained at homes and at health facilities.

# **Results**

A total of 5204 children were enrolled at home; 3436 were under 24 months of age at the start of surveillance, 1685 were born during the surveillance period and 83 migrated into the area. Enrolled children aged 2–35 months contributed 4849 years of observation between 1 September 2001 and 31 December 2002. Health workers reported 32 deaths among children aged 2–35 months between 1 January and 31 December 2002. Of these deaths, 23 were in infants aged 2–11 months.

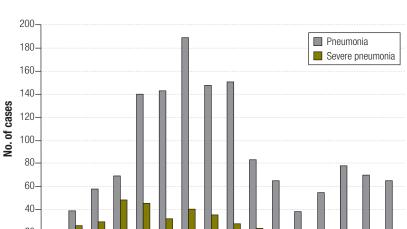


Fig. 1. Children (n = 1260) with pneumonia and severe pneumonia presenting to 19

31 December 2002<sup>a</sup>

health facilities, Punial and Ishkoman valleys, Pakistan, 1 September 2001 to



<sup>a</sup> Surveillance was fully established between 1 November 2001 and 31 December 2002.

Health-centre staff correctly classified 1397 (99%) episodes of pneumonia in 949 children, and 377 (72%) episodes of severe pneumonia in 311 children. Multiple episodes of the disease, separated by at least 4 weeks of wellness, occurred in 262 children (28%) with pneumonia and 24 children (8%) with severe pneumonia. The annual community-based incidence was 29.9 per 100 child-years of observation for pneumonia and 8.1 per 100 child-years of observation for severe pneumonia among children aged 2-35 months in the Punial and Ishkoman valleys (Table 1). Age and gender were similar among children with pneumonia and severe pneumonia, but children with severe pneumonia were more likely to have received antibiotics before treatment at health facilities than those with pneumonia (Table 2). The peak incidence of pneumonia occurred from January to May (Fig. 1). The highest incidence occurred at 4 months of age and decreased with increasing age (Fig. 2).

In the regression analysis (adjusting for altitude, gender and number of children aged under 36 months in the household), the incidence rate ratio (IRR) was highest for children aged 2–5 months compared with children aged 24–35 months (Table 3). Children living at an altitude of 1980–2285 m had a higher IRR for pneumonia (IRR: 1.66; 95% confidence interval, CI: 1.45–1.90) than children living at an altitude of 1675–1980 m, but this ratio decreased at higher altitudes. The incidence in males was slightly higher than in females (IRR: 1.14; 95% CI: 1.01–1.29). The incidence rate among children living in households with one or more children under 36 months did not differ significantly from that among children living in households that did not include such children.

# Discussion

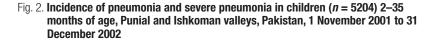
The incidence of pneumonia and severe pneumonia combined (38 per 100 child-years of observation) among children aged 2-35 months living in this area is higher than the rate of 22 per 100 child-years of observation reported for children in Lahore, which is at a lower altitude. Possible explanations for this high rate could include indoor air pollution by wood fires, harsh winters (which necessitate greater time indoors in overcrowded homes), over-diagnosis because of increased baseline respiratory rates at high altitudes, and a true increased risk of disease associated with altitude.

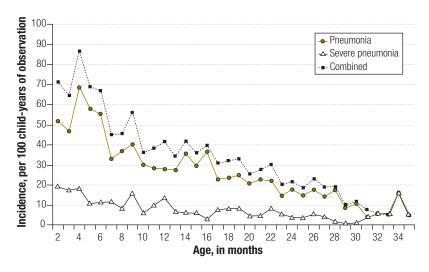
Much of the research conducted on the physiological responses of children at high altitude has come from populations living above 3048 m in the Peruvian Andes. Reuland et al. showed that

Research Childhood pneumonia at high altitudes in Pakistan

it takes neonates 3 to 4 years to adapt physiologically to these high altitudes through compensatory mechanisms such as increased ventilation, cardiac output and vital capacity, and a shift in the oxyhaemoglobin affinity curve.<sup>30</sup> The degree to which these findings from Andean populations living above 3048 m may apply to children in the Punial and Ishkoman valleys, who live at 1675–2590 m, is uncertain.

High baseline respiratory rates among infants and young children residing at high elevations could contribute to the high pneumonia incidence rates reported, since disease that might not be classified as pneumonia at lower altitudes could result in respiratory rates sufficient to be classified as pneumonia at higher altitudes. Many children in developing countries have underlying asthma that predisposes to fast breathing even with mild illness.<sup>31</sup> This may explain why almost one-third (28%) of children with pneumonia had recurrent episodes; however, even after accounting for this possibility, the incidence of pneumonia is still high (20 cases per 100 child-years of observation). The strongest evidence for a true increased risk of disease at high altitudes in our setting is the high rate of severe pneumonia (8 per





100 child-years of observation), which does not depend on the respiratory rate at the time of illness. All pneumonias reported at altitudes above 2590 m were severe cases; this is likely to reflect the difficult terrain and limited access to health centres at these altitudes, with families only seeking treatment when children are severely ill.

Almost all households (98%) used indoor wood-stove (*bukhari*) fires for

Table 3. Pneumonia IRRs by age among 5204 children, adjusted for altitude, number of children under 36 months of age in household and gender, Punial and Ishkoman valleys, Pakistan, 1 November 2001 to 31 December 2002

| Covariate                                    | IRR   | 95% CI    |
|--|-------|-----------|
| Age group, in months                         |       |           |
| Reference = $24-35$                          |       |           |
| 2 to < 6                                     | 4.33* | 3.53-5.32 |
| 6 to < 12                                    | 3.27* | 2.66-4.03 |
| 12 to < 18                                   | 2.69* | 2.18-3.32 |
| 18 to < 24                                   | 2.04* | 1.64-2.53 |
| Altitude range, in metres                    |       |           |
| Reference = $1675 - 1980$                    |       |           |
| 1980–2285                                    | 1.66* | 1.45-1.90 |
| 2286–2590                                    | 1.09  | 0.92-1.30 |
| > 2590                                       | 0.16* | 0.08-0.32 |
| No. of children < 36 months old in household |       |           |
| Reference $= 0$                              |       |           |
| 1–2  | 0.99  | 0.84-1.17 |
| ≥3   | 1.03  | 0.78-1.35 |
| Gender                                       |       |           |
| Reference = female                           |       |           |
| Male   | 1.14* | 1.01-1.29 |

CI, confidence interval; IRR, incidence rate ratio.

\* P < 0.05 in Poisson regression analysis.

cooking and warming the sleeping area throughout the year. A household socioeconomic survey conducted in 2002 in this area revealed an average of 9.5 persons and 2.7 rooms per household.<sup>32</sup> The mean number of persons per room was 3.5. However, children living in households with three or more other children under 3 years of age did not have higher rates of pneumonia than those living in households with no infants.

Limitations of the present study include the absence of data on nutritional status as a possible cofactor and lack of continuing home-based enrolment in two villages, each with about 20 households. We do not believe there was a problem with the classification of sick children by health workers because of the close supervision, repeat training and comparison of assessments and classifications.

The lack of bacteriology services and small number of blood culture results available during the course of surveillance in the Punial and Ishkoman valleys limit our ability to determine the proportion of pneumonia cases attributable to specific pathogens. Viral infections, especially respiratory syncytial virus infection and influenza, are likely to be responsible for a large proportion of pneumonia cases in young children living in these communities. Efforts were under way to improve diagnostic bacteriology capabilities in health centres, but conflicts in neighbouring Afghanistan and terrorist attacks in other parts of Pakistan during 2002 resulted

in withdrawal of donor support for the second phase of this project.

Further studies are needed to determine the causes of the high burden of disease from pneumonia in these communities. Nevertheless, consideration should be given to the introduction and evaluation of a vaccine to prevent *Streptococcus pneumoniae* because this remains the most common cause of bacterial pneumonia in children aged 2 months to 5 years.<sup>33</sup>

#### Acknowledgements

We thank the people of Punial and Ishkoman for their trust in our effort and their incomparable hospitality. We thank the following for their field work on this study: female government health workers from the National Health Worker Program (NHW); NHW program supervisors; dispensers and medical officers; Aga Khan Health Services Pakistan (AKHSP) female health visitors and medical officers; and Hina Rehman, Irum Khan and Jawad Kayani, elective students from the Aga Khan University (AKU). We acknowledge the technical contributions of Zeba Rasmussen from AKU; Stephen Hayes and Peter Hatcher from the AKHSP; and Syed Jaffar Hussain from the WHO IMCI team in

Islamabad. We are grateful to the following for their administrative support: Wazir Khan, District Health Officer of Ghizer District; Mehboob Khan, Logisitical Officer for the government NHW Programme in Ghizer; Nazim Somani from AKHSP Northern Areas; and Masood Kadir from AKU.

**Funding:** SmithKline Beecham, Fondation Pasteur Merieux and Aventis Pasteur.

Competing interests: None declared.

#### Résumé

# Forte incidence de la pneumonie infantile dans les régions de haute altitude du Pakistan : étude longitudinale de cohorte

**Objectif** Déterminer l'incidence de la pneumonie et de la pneumonie sévère chez les enfants vivant à haute altitude au Pakistan.

**Méthodes** On a mené une étude longitudinale de cohorte dans laquelle 99 agents de santé féminins de l'Etat, exerçant dans les vallées de Punial et d'Ishkoman (District de Ghizer, zones septentrionales du Pakistan), ont recruté des enfants à domicile, effectué des visites domiciliaires toutes les 2 semaines et orienté activement les enfants malades vers 15 centres de santé. Le personnel des centres de santé a utilisé les critères de gestion intégrée des maladies infantiles pour dépister l'ensemble des enfants malades de 2 à 35 mois et identifier ceux atteints de pneumonie ou de pneumonie sévère.

**Résultats** Les agents de santé communautaires ont recruté à leur domicile 5204 enfants susceptibles de participer à l'étude et les ont suivis sur une période de 14 mois, qui s'est achevée le 31 décembre 2002. Le personnel des centres de santé a identifié 1397

cas de pneumonie et 377 cas de pneumonie sévère parmi les enfants recrutés de 2 à 35 mois. Parmi les enfants signalés comme atteints de pneumonie, 28 % ont présenté plusieurs épisodes de cette maladie. Le taux d'incidence pour 100 années-enfants d'observation était de 29,9 pour la pneumonie et de 8,1 pour la pneumonie sévère. Les facteurs associés à une forte incidence de la pneumonie étaient le jeune âge, le sexe masculin et la vie à haute altitude.

**Conclusion** Les taux d'incidence de la pneumonie dans les zones septentrionales du Pakistan sont bien plus élevés que ceux signalés dans ce pays à plus faible altitude et sont similaires à ceux relevés dans les régions de haute altitude d'autres pays en développement. Il faudrait entreprendre d'autres études pour déterminer les causes de la pneumonie dans ces communautés de haute montagne. Il faudrait néanmoins aussi envisager l'introduction d'une vaccination à un âge précoce par des vaccins connus pour prévenir cette maladie.

## Resumen

#### Alta incidencia de neumonía en la niñez a grandes altitudes en el Pakistán: estudio longitudinal

**Objetivo** Determinar la incidencia de neumonía y neumonía grave entre los niños de zonas situadas a gran altitud en el Pakistán.

**Métodos** En los valles de Punial e Ishkoman (distrito de Ghizer, en el norte del país) se llevó a cabo un estudio longitudinal de cohortes en el que 99 funcionarias de salud reclutaron a niños visitados en sus hogares, realizaron visitas a domicilio cada 2 semanas y derivaron activamente a los niños enfermos a 15 centros de salud. El personal de esos centros utilizó los criterios de la Atención Integrada a las Enfermedades Prevalentes de la Infancia para someter a tamizaje a todos los niños enfermos de 2 a 35 meses de edad e identificar a los que sufrían neumonía o neumonía grave.

**Resultados** Las trabajadoras sanitarias de la comunidad incluyeron en el estudio a 5204 niños elegibles identificados en sus hogares a lo largo de un periodo de 14 meses que concluyó el 31 de diciembre de 2002. El personal de los centros de salud detectó 1397 casos de neumonía y 377 casos de neumonía grave entre los niños participantes de 2 a 35 meses. Entre los niños a los que se diagnosticó neumonía, el 28% presentaron varios episodios. Las tasas de incidencia por 100 niños-año de observación fueron de 29,9 para la neumonía y 8,1 para la neumonía grave. Los factores asociados a una elevada incidencia de neumonía fueron una más corta edad, el sexo masculino y el hecho de vivir a gran altura.

**Conclusión** Las tasas de incidencia de neumonía en las zonas del norte del Pakistán son mucho mayores que las observadas a más baja altitud en el país, y similares a las habituales a grandes alturas en otros países en desarrollo. Es necesario realizar más estudios para determinar las causas de la neumonía en esas comunidades de alta montaña. Sin embargo, debe estudiarse la posibilidad de introducir tempranamente las vacunas que se sabe que previenen dicha enfermedad.

# ملخص

# معدل مرتفع لحدوث الالتهاب الرئوي بين الأطفال في المرتفعات العالية في باكستان: دراسة أترابية طولانية

ا**لهدف:** التعرُّف على معدل حدوث الالتهاب الرئوي والالتهاب الرئوي الوخيم بن الأطفال الذين يعيشون في المرتفعات الشاهقة في باكستان.

الطريقة: أجريت دراسة أترابية طولانية شارك فيها 99 من العاملات الصحيات الحكوميات في واديي بونيال ويشكومان (مقاطعة غيزار في المناطق الشمالية من باكستان)، حيث قمن بزيارة الأطفال في بيوتهم كل أسبوعين وإحالة المرضى منهم إلى 15 مركزاً صحياً. وقد استخدم العاملون في المراكز الصحية معايير التدبير المتكامل لأمراض الأطفال لفحص جميع الأطفال المرضى الذين تتراوح أعمارهم بين 2 و35 شهراً والتعرف على الأطفال المصابين بالالتهاب الرئوى والمصابين بالالتهاب الرئوى الوخيم.

**الموجودات:** أدرجت العاملات الصحيات المجتمعيات 5204 طفلاً مؤهلاً للدراسة من خلال زيارتهم في منازلهم ومتابعتهم لمدة 14 شهراً انتهت في 31 كانون الأول/ديسمبر 2002. وقد تعرف العاملون على 1397 حالة التهاب رئوي و377 حالة التهاب رئوي وخيم بين الأطفال المشاركين في الدراسة ممن

تتراوح أعمارهم بين 2-35 شهراً. ومن بين الأطفال الذين أبلغ عن إصابتهم بالالتهاب الرئوي كان لدى 28% منهم نوبات متعددة، وبلغ معدل الوقوعات لكل 100 طفل – سنوات من الملاحظة 29.9 للالتهاب الرئوي و8.1 للالتهاب الرئوي الوخيم. وشملت العوامل المرتبطة بارتفاع معدل وقوعات الالتهاب الرئوى، العمر الصغير والذكورة والحياة في المرتفعات العالية.

الاستنتاج: إن معدلات حدوث الالتهاب الرئوي في المناطق الشمالية من باكستان أعلى بكثير من المعدلات المبلغ عنها في المناطق الأقل ارتفاعاً في البلاد وهي مشابهة لما هي عليه في مناطق المرتفعات العالية في البلدان النامية الأخرى. وهناك حاجة إلى إجراء مزيد من الدراسات للتعرف على أسباب الالتهاب الرئوي في المجتمعات التي تقطن الجبال المرتفعة. ومع ذلك فإن الإدخال الباكر للقاحات المعروفة أنها تقي من الالتهاب الرئوي يعد أمراً جديراً بالاعتبار.

#### References

- Pakistan Demographic Health Survey 1998. Islamabad: National Institute of Population Studies; 1998.
- Black RE, Morris SS, Bryce J. Child survival I: where and why are 10 million children dying every year? *Lancet* 2003;361:2226-34. PMID:12842379
- Khan AJ, Khan JA, Akbar M, Addiss DG. Acute respiratory infections in children: a case management intervention in Abbottabad District, Pakistan. *Bull World Health Organ* 1990;68:577-85. PMID:2289294
- Marsh D, Majid N, Rasmussen Z, Mateen K, Khan AA. Cause-specific child mortality in a mountainous community in Pakistan by verbal autopsy. *J Pak Med Assoc* 1993;43:226-9. PMID:8114258
- 5. Annual report 2001, Pakistan Northern Areas and Chitral. Islamabad: Aga Khan Health Service; 2002.
- Selwyn BJ. The epidemiology of acute respiratory tract infection in young children: comparison of findings from several developing countries. *Rev Infect Dis* 1990;12 Suppl 8:S870-88. PMID:2270410
- Monto AS. Studies of the community and family: acute respiratory illnesss and infection. *Epidemiol Rev* 1994;16:351. PMID:7713184
- Rudan I, Tomaskovic L, Boschi-Pinto C, Campbell H; WHO Child Health Epidemiology Reference Group. Global estimate of the incidence of clinical pneumonia among children under five years of age. *Bull World Health Organ* 2004;82:895-903. PMID:15654403
- Lanata CF, Quintanilla N, Verastegui HA. Validity of a respiratory questionnaire to identify pneumonia in children in Lima, Peru. *Int J Epidemiol* 1994; 23:827-34. doi:10.1093/ije/23.4.827 PMID:8002198
- Lehmann D. Epidemiology of acute respiratory tract infections, especially those due to Haemophilus influenzae, in Papua New Guinean children. *J Infect Dis* 1992;165 Suppl 1:S20-5. PMID:1588165
- Black RE, Brown K, Becker S, Yunus M. Longitudinal studies of infectious diseases and physical growth of children in rural Bangladesh. *Am J Epidemiol* 1982;115:305-14. PMID:7064969
- James JW. Longitudinal study of the morbidity of diarrheal and respiratory infections in malnourished children. Am J Clin Nutr 1972;25:690-4.
- Barreto ML, Santos LM, Assis AM, Araújo MP, Farenzena GG, Santos PA, et al. Effect of vitamin A supplementation on diarrhoea and acute lower respiratory tract infections in young children in Brazil. *Lancet* 1994;344:228-31. doi:10.1016/S0140-6736(94)92998-X PMID:7913157
- Black RE. Zinc deficiency, infectious disease and mortality in the developing world. J Nutr 2003;133 5 Suppl 1;1485S-9S. PMID:12730449
- Oyejide CO, Osinusi K. Acute respiratory tract infection in children in Idikan Community, Ibadan, Nigeria: severity, risk factors and severity of occurrence. *Rev Infect Dis* 1990;12 Suppl 8:S1042-6. PMID:2270403
- Mulholland K. Measles and pertussis in developing countries with good vaccine coverage. *Lancet* 1995;345:305-7. PMID:7837867
- Tupasi TE, Leon LE, Lupisan S, Torres CU, Leonor ZA, Sunico ES, et al. Patterns of acute respiratory tract infection in children: a longitudinal study in a depressed community in Metro Manila. *Rev Infect Dis* 1990;12:S940-9.

- Ruutu P, Halonen P, Meurman O, Torres C, Paladin F, Yamaoka K, et al. Viral lower respiratory tract infections in Filipino children. *J Infect Dis* 1990; 161:175-9. PMID:2153734
- Victora CG, Kirkwood BR, Ashworth A, Black RE, Rogers S, Sazawal S, et al. Potential interventions for the prevention of childhood pneumonia in developing countries: improving nutrition. *Am J Clin Nutr* 1999;70:309-20.
- Lopez de Romana G, Brown KH, Black RE, Kanashiro HC. Longitudinal studies of infectious diseases and physical growth of infants in Huascar, an underprivileged peri-urban community in Lima, Peru. *Am J Epidemiol* 1989;129:769-84. PMID:2923124
- Smith KR, Samet JM, Romieu I, Bruce N. Indoor air pollution in developing countries and acute lower respiratory infections in children. *Thorax* 2000;55:518-32. doi:10.1136/thorax.55.6.518 PMID:10817802
- Armstrong JR, Campbell H. Indoor air pollution exposure and lower respiratory infections in young Gambian children. *Int J Epidemiol* 1991;20:424-9. PMID:1917245
- Zaman S, Jalil F, Karlberg J, Hanson LA. Early child health in Lahore, Pakistan: VI. Morbidity. *Acta Paediatr Suppl* 1993;82 Suppl 391;63-78. doi:10.1111/j.1651-2227.1993.tb12907.x PMID:8219468
- Jalil F, Lindblad BS, Hanson LA, Khan SR, Ashraf RN, Carlsson B, et al. Early child health in Lahore, Pakistan: I. Study design. *Acta Paediatr Suppl* 1993;82 Suppl 391;3-16. doi:10.1111/j.1651-2227.1993.tb12902.x PMID:8219465
- Khan SR, Jalil F, Zaman S, Lindblad BS, Karlberg J. Early child health in Lahore, Pakistan: X. Mortality. *Acta Paediatr Suppl* 1993;82 Suppl 391;109-17. doi:10.1111/j.1651-2227.1993.tb12911.x PMID:8219459
- Nizami SQ, Bhutta ZA, Hasan R. Incidence of acute respiratory infections in children 2 months to 5 years of age in periurban communities in Karachi. *J Pak Med Assoc* 2006;56:163-7. PMID:16711336
- Pechere JC, ed. Community acquired pneumonia in children. Worthing: Cambridge Medical Publications; 1995.
- 28. 2001 annual report. Islamabad: Aga Khan Health Service; 2002.
- Integrated Management of Childhood Illness. Geneva: World Health Organization; 2006. ISBN 9241546441. Available from: www.who.int/childadolescent-health/publications/publMCl.htm [accessed on 6 February 2007].
- Reuland DS, Steinhoff MC, Gilman RH, Bara M, Olivares EG, Jabra A, et al. Prevalence and prediction of hypoxemia in children with respiratory infections in the Peruvian Andes. *J Pediatr* 1991;119:900-6. PMID:1960604
- Heffelfinger JD, Davis TE, Gebrian B, Bordeau R, Schwartz B, Dowell SF. Evaluation of children with recurrent pneumonia diagnosed by World Health Organization criteria. *Pediatr Infect Dis J* 2002;21:108-12. doi:10.1097/00006454-200202000-00005 PMID:11840076
- Hussain H, Waters H, Khan A, Omer S, Halsey N. Economic analysis of childhood pneumonia in Northern Pakistan. *Health Policy Plan* 2008; 23:438-42. doi:10.1093/heapol/czn033 PMID:18755733
- Shann F. Etiology of severe pneumonia in children in developing countries. *Pediatr Infect Dis* 1986;5:247-52. PMID:3952013