Risk factors for childhood pneumonia among the urban poor in Fortaleza, Brazil: a case-control study

W. Fonseca,¹ B.R. Kirkwood,² C.G. Victora,³ S.R. Fuchs,⁴ J.A. Flores,⁵ & C. Misago⁶

Reported are the results of a case-control study carried out between July 1989 and June 1990 in Fortaleza city, Ceará State, Brazil, to determine the factors that place young children living in urban slum conditions at increased risk of contracting pneumonia. Cases were 650 under-2-year-olds with a radiological diagnosis of pneumonia who were recruited at the main paediatric hospital in the city over a full calendar year. Agematched controls were recruited from the neighbourhood where the cases lived. Cases and controls were compared with respect to a variety of sociodemographic, environmental, reproductive, nutritional, and morbidity factors, and a risk factor questionnaire was administered to the mother of each child or to the child's normal guardian. Cases and controls were also weighed and measured.

Malnutrition was the most important risk factor for childhood pneumonia in the study population, with weight-for-age, height-for-age, and weight-for-height also being important risk factors. In view of the high prevalence of stunting in the study population, there is an urgent need to reduce the level of malnutrition as a priority.

Attendance at a day care centre was also associated with a high odds ratio. In view of the growing numbers of children attending day care centres in both developing and developed countries, it is essential that ways be identified to improve the design and management of such centres in order to minimize the risk of pneumonia.

Increased risks of childhood pneumonia were also associated with low birth weight, non-breast-feeding, crowding, high parity, and incomplete vaccination status, but not with socioeconomic status or environmental variables. Finally, children who had suffered from previous episodes of wheezing or been hospitalized for pneumonia had a greater than threefold increased risk of contracting the disease.

Introduction

Acute respiratory infections (ARI) are one of the leading causes of childhood morbidity and mortality in developing countries, accounting for approximately a third of the 15 million deaths that occur annually among under-5-year-olds (1). The majority (75%) of these ARI deaths are due to pneumonia

unassociated with measles.^a Case management together with vaccination (measles, diphtheria, pertussis) is the main strategy for ARI control (2). Detailed understanding about the epidemiology of ARI is needed both to develop preventive programmes and to identify high-risk groups in order to target more effectively case-management interventions.

Among the factors that have been postulated to increase the risk of ARI among children in developing countries are the following: low birth weight, failure to breast-feed, malnutrition, indoor air pollution, and sociodemographic factors such as large family size, short birth interval, low income, low level of parental education, poor housing, and inappropriate child care practices (2, 3). However, in developing countries evidence on the association between these factors and pneumonia in children is

¹ Clinical Research Fellow, Universidade Federal do Ceará, CE, Brazil; and Institute of Woman and Child Health, Rua Silva Jatay n° 15 sala 801, CEP 60165-070, Fortaleza, Ceará, Brazil. Requests for reprints should be sent to this author at the latter address.

² Professor and Head, Maternal and Child Epidermiology Unit, London School of Hygiene and Tropical Medicine, London, England.

³ Professor, Universidade Federal de Pelotas, Pelotas, CE, Brazil.

⁴ Research Fellow, Universidade Federal de Pelotas, Pelotas, CE, Brazil.

⁵ Radiologist, Hospital Pediatrico Santo Antonio, Porto Alegre, RS, Brazil.

⁶ Research Fellow, Maternal and Child Epidemiology Unit, London School of Hygiene and Tropical Medicine, London, England. Reprint No. 5692

^{*} Programme for the Control of Acute Respiratory Infections: programme report, 1988. Unpublished document WHO/ARI/89.3, 1990.

scarce. In this article, we report the results of a casecontrol study carried out to elucidate the major risk factors for childhood pneumonia among the urban poor in Fortaleza, north-east Brazil.

Methods

Study site

Fortaleza, the capital of Ceará State, is located at latitude 3°S in a tropical zone; it includes the metropolitan area and greater Fortaleza and has a population of 2 million. The area's climate is determined by its proximity to the equator and its low altitude (sea level). The temperature is high throughout the year (25–38°C). The economy of the metropolitan area consists almost entirely of fishing, the textile industry, and commerce, with a heavy reliance on tourism. Patients with pneumonia were recruited for the study from the outpatient and inpatient departments of the Hospital Infantil Albert Sabin, the largest public paediatric hospital in the metropolitan area, catering mostly to low-income families. At the time of the study the infant mortality rate was approximately 90 per 1000 live births. According to official estimates, over half of the population live in favelas (shanty towns). A recent survey of 8000 families in Ceará State showed that respiratory infections are the second most important infectious cause of infant death (11%) referred to by mothers and the commonest reason for using health services (38%).^b

Sample size

Between 1 July 1989 and 30 June 1990 a total of 650 cases and 650 matched controls were recruited to the study. This gives a 90% power for detecting a relative risk of ≥ 1.6 as significant at the 5% level if the prevalence of exposure among controls is 15–75%. (4). Such a sample size will detect a relative risk of ≥ 2 as significant for a prevalence of exposure in the range 4–90%.

Selection of cases

Cases were children aged 0–23 months with radiologically confirmed pneumonia who were seen at the outpatient clinic of the paediatric hospital. It is routine practice to give all children with suspected pneumonia a chest X-ray. Only children whose chest X-ray showed evidence of pulmonary infiltration were included in the study. All the X-ray results were examined by a paediatric radiologist.^c Children presenting with wheezing or a recent history of aspiration of a liquid or a foreign body were excluded, as were those with measles or underlying diseases such as symptomatic congenital heart disease, congenital malformation, cerebral palsy, cystic fibrosis or acquired immunodeficiency syndrome (AIDS). Approximately 800 children were recruited as potential cases and 4% were excluded using these criteria; also excluded were all children who died during the recruitment period (<2%).

The selection of cases took place over a full calendar year to cover seasonal variations in the incidence and etiology of pneumonia, with the same number of cases (12 or 13) being selected each week. Since there were more children with pneumonia than were required for the study, cases were selected on only 3 days per week, as described below, so that all days of the week were represented. In the first week of recruitment the first 12 (or 13) children with a chest X-ray diagnosis of pneumonia who presented on Monday, Tuesday, or Wednesday were entered. The following week, case selection took place from Thursday to Saturday, and the next week from Sunday to Tuesday. This pattern was continued until at the end of the month all days of the week had similar proportional representations. For logistic reasons, the study was restricted to children living in the metropolitan areas of the city.

Selection of controls

Controls were children recruited from the same neighbourhood as the cases. In order to avoid any gross imbalance in age distribution, the controls were stratum matched to cases according to age group (0-5, 6-11 and 12-23 months). Wide age groups were chosen so that matching could be easily achieved. It should be noted that this approach does not preclude the analysis of risks associated with smaller age intervals. Adjustments of any remaining imbalance in the age distribution were made in the statistical analyses as required, e.g., in the analysis of breast-feeding.

One neighbourhood control was selected for each case, as described below. A female field worker located the home of each case using the address supplied to the hospital. She then asked at every neighbouring house whether or not there was a child

^b [*The health of children in Ceará: a study of 8000 families*]. Fortaleza, Ceará. UNICEF unpublished document, 1991 (in Portuguese).

^c Respiratory infections in children: management at small hospitals. Background notes and a manual for doctors. Unpublished document WHO/RSD/86.26, 1987.

of approximately the same age as the case; the first suitable child that was identified in this way served as the control. All empty houses were checked with the next-door neighbour to determine whether there was a child who might be suitable as a control. If necessary, the interviewer returned to the house to reach any absent child, in order to minimize the possibility of selection bias arising from failure to recruit such children as controls. Children were not selected as controls if they had a respiratory rate of ≥ 50 breaths per minute (infants) or ≥ 40 breaths per minute for older children; those with symptoms of measles or pertussis in the preceding 10 days were also excluded. Mothers were asked to specify the type of health service (government or private) to which they would take their child if he/she had pneumonia. In order to reduce further the possibility of any selection bias, only those children whose mothers said they would attend government services were included as controls.

Assessment of risk factors

The mothers (or guardians) of potential cases were first contacted at the clinic before the children were X-rayed and were asked whether they would participate in the study. After the exclusion criteria were applied, detailed information on their place of residence was collected. More than 99% of the houses were located and only one mother refused to have her child participate in the study.

The main clinical and laboratory findings for cases were recorded on a specially designed form. Cases were weighed and measured at admission or clinic consultation; controls were weighed and measured at home. The children were weighed naked on a calibrated portable scale of precision $\pm 100g$ (CMS Measuring Equipment, model PBW-235) and measured to the nearest mm using an AHRTAG baby length measure. A risk factor questionnaire was also administered to the mother of each case and control or to the child's normal guardian, either in the clinic for cases admitted for treatment (30%) or at home for the other cases and for all controls. The home visit lasted 40–50 minutes and was carried out as soon as possible after the child's recruitment.

Data recording and analysis

Standardized, precoded questions were used for most variables. The data were entered onto an IBMcompatible microcomputer in Fortaleza, using dBase III+. Range and consistency checks were carried out for all variables and the data were cleaned and edited using dBase III+, SPSS/PC+, Epi-Info 5.1, and Egret software.

Risk factors for childhood pneumonia in Brazil

The analyses performed included simple tabulations of all risk and confounding factors according to case-control status. Cases and controls were matched by neighbourhood and age in all analyses. The odds ratio was estimated from the ratio of the discordant pairs, i.e., the number of pairs where the case was exposed and the matched control unexposed, divided by the number of pairs where the case was unexposed and the control exposed (5). McNemar's χ^2 test was used to assess the strength of the association; also, two-tailed significance tests were employed.

For risk factors with several exposure categories, conditional logistic regression was used to determine whether the risk of pneumonia increased linearly with the level of exposure, and if so whether there was any evidence of departure from linearity. Conditional logistic regression was also used to investigate the effect of risk factors, after controlling for potential confounding variables (6). A stepwise procedure was not used; instead, variables for inclusion in the model were selected on an a-priori basis using probable links between them and the results of the univariate analyses. Socioeconomic variables such as income and educational level of the father and mother may affect, directly or indirectly, all other groups of risk factors with the exception of sex and age. Such variables were incorporated in the multivariate analyses, including those that were not significant in the crude analysis. Other variables were included in the model if there was a clear association — including a dose-response pattern for variables with three or more categories --- the variable concerned was used in the model; statistical significance was an additional criterion for retaining a variable. The confounding variables included in each model of the multivariate analysis are shown in Table 1. Homogeneity of the rate ratios across strata was tested using the method described by Breslow & Day (7).

Variables with missing values were treated as follows. In instances where there were a substantial number of missing values, case-control pairs were not excluded; instead, missing values were included as a separate category in the exposure code, and relative risks were calculated for this category in the normal way. Where data were missing for less than 1% of cases or controls, the case-control pairs affected were excluded.

Results

Table 1 summarizes the strength of the association between each of the main risk factors investigated and childhood pneumonia, in descending

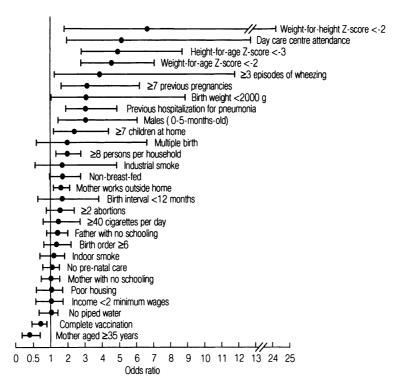


Fig. 1. Plot showing 95% confidence intervals of the odds ratios for risk factors for childhood pneumonia.

order of the estimated odds ratios. The data shown include control for potential confounding variables as appropriate, together with the 95% confidence intervals (CI) (Fig. 1) and the prevalence of the occurrence of the risk factor in the control group.

Anthropometric status

Malnutrition was the most important risk factor for childhood pneumonia in the study population, with all three anthropometric indices — low weight-forheight, low height-for-age, and low weight-for-age all appearing at the top of Table 1. A substantial proportion of the control children were severely stunted, 8.4% having a height-for-age Z-score <-3with an estimated associated odds ratio of 5.05. A similar proportion (9.5%) had weight-for-age Zscores <-2, with an estimated odds ratio of 4.57. Although associated with the highest overall odds ratio (6.75), the occurrence of wasting in the study population was less common — 0.9% of control children had a weight-for-height Z-score <-2. In addition to the large estimated odds ratios for the lowest categories, all three anthropometric indices showed highly significant trends of increasing risk of pneumonia with decreasing Z-score (see Table 2). The majority of children, even the controls, exhibited some degree of undernutrition, and the increased risk of pneumonia was apparent (and statistically significant) even in the mildest category. Children with a Z-score between 0 and -1 for any of the three indices had a 1.7–1.8 times greater risk than those in the baseline categories (Z-score ≥ 0).

Low birth weight

Low birth weight was also significantly associated with pneumonia, with an odds ratio of 3.16 (95% CI = 1.12, 8.94) for babies of birth weight <2000g relative to those weighing \geq 2500g. Although important, this odds ratio is lower than that for current

WHO 96063

Risk factors for childhood pneumonia in Brazil

Risk factor	% prevalence in control group	Odds ratio	95% Cl 1.88, 24.27	
Weight-for-height Z-score <-3	0.9	6.75 ^₅		
Day care centre attendance	1.2	5.22*	2.13, 12.79	
Height-for-age Z-score <-3	8.4	5.05 ^b	2.92, 8.74	
Weight-for-age Z-score <-3	9.5	4.57 ^b	2.93, 7.13	
≥3 episodes of wheezing	0.9	3.91°	1.29, 11.92	
≥7 previous pregnancies	5.8	3.22 ^d	1.66, 6.24	
Birth weight <2000 g	1.0	3.16°	1.12, 8.94	
Previous hospitalization for pneumonia	5.4	3.08°	1.95, 4.86	
Males (0-5-months-old)	49.4	2.98	1.46, 6.10	
≥7 children at home	3.9	2.36′	1.26, 4.43	
Multiple birth	1.1	2.00	0.60, 6.64	
≥8 persons in household	20.3	1.99 ⁶	1.42, 2.80	
Industrial smoke	9.7	1.72	0.61, 4.90	
Non-breast-feeding	72.6	1.699	1.02, 2.80	
Mother works outside home	25.1	1.58 ⁶	1.21, 2.07	
Birth interval <12 months	3.2	1.57	0.64, 3.81	
≥2 abortions	4.9	1.47	0.92, 2.37	
≥40 cigarettes per day	5.6	1.44	0.78, 2,66	
Father with no schooling	18.5	1.36	0.93, 1.98	
Birth order ≥6	11.0	1.32	0.79, 2.22	
Indoor smoke	9.6	1.14	0.71, 1.81	
No antenatal care	13.2	1.07	0.78, 1.48	
Mother with no schooling	15.4	1.06	0.76, 1.50	
Poor housing	12.0	1.05	0.63, 1.73	
Income < twice minimum wage	60.0	1.02	0.60, 1.72	
No piped water	40.6	0.99	0.70, 1.39	
Complete vaccination	62.5	0.68 ^b	0.52, 0.88	
Mother aged ≥35 years	11.7	0.37*	0.20, 0.67	

Table 1: Su	mmary	of risk	factors	for	childhood	pneumonia,	arranged	in
descending	order o	of the es	stimated	odd	ls ratio	-	_	

^a Model 1: income, education of the father and mother.

^b Model 2: model 1, plus previous episode of pneumonia.

° Model 3: model 1, plus sex, age, mother's age, crowding, nutritional status (height-for-age

Z-score), previous wheezing or pneumonia.

^d Model 4: model 1, plus sex and age.

Model 5: model 1, plus maternal age, number of abortions and previous stillbirths.

' Model 6: model 1, plus mother's age and crowding.

⁹ Model 7: model 1, plus sex, age and low birth weight.

ⁿ Model 8: model 1, plus number of previous pregnancies.

nutritional status, and in the study population relatively few children had a birth weight less than this. Children whose birth weights lay in the intermediate range (2000–2499g) were at an increased but nonsignificant risk (OR = 1.38). The trend of the association between decreasing birth weight and increasing risk of pneumonia was significant (P = 0.01).

Non-breast-feeding

The third nutritionally related risk factor, nonbreast-feeding, was also significantly associated with an increased risk of pneumonia, with an estimated OR = 1.69 (P = 0.01). Since approximately threequarters of the control children were non-breast-fed, on a population basis, non-breast-feeding probably plays an important role in causing the high pneumonia rates in the study population.

Child care practices

Two variables related to child care practices emerged as strong risk factors for childhood pneumonia in the study population. Attendance at a day care centre had the second highest odds ratio (estimated at 5.22) of all the risk factors studied. Although current use of day care centres is low in this poor urban population (only 1.2% of control children attended a centre), the level will probably grow dramatically over the next few years, since more day care facilities are planned.

Having a working mother was also associated with an increased risk of pneumonia. About a quar-

Table 2: Anthropometric status as a risk factor for childhood pneumonia

Risk factor (Z-score)	No. of cases		Odds ratio		
		No. of controls	Unadjusted ^e	Adjusted ^b	
Height-for-age					
≥0	63 (9.7) ^c	113 (17.4)	1.00	1.00	
-0.01 to -1	149 (22.9)	172 (26.5)	1.73; <i>1.17–2.55</i> ^d	1.81; 1.21-2.70	
-1.01 to -2	184 (28.3)	175 (26.9)	2.17; 1.48-3.19	2.09; 1.41-3.11	
-2.01 to -3	149 (22.9)	135 (20.8)	2.56; 1.66-3.94	2.39; 1.53-3.74	
<-3	105 (16.2)	55 (8.4)	5.09; 3.01-8.60	5.05; 2.92-8.74	
Likelihood ratio test (4 df)			43.09; <i>P</i> < 0.001	37.03; <i>P</i> < 0.001	
(trend, 1 df)			38.94; <i>P</i> < 0.001	30.94; <i>P</i> < 0.001	
Weight-for-height					
≥0	337 (51.8)	434 (66.8)	1.00	1.00	
-0.01 to -1	203 (31.2)	154 (23.7)	1.80; <i>1.38–2.36</i>	1.69; <i>1.28–2.24</i>	
-1.01 to -2	92 (14.2)	56 (8.6)	2.30; 1.56-3.39	2.08; 1.39-3.12	
<-2	18 (2.8)	6 (0.9)	6.80; 1.94-23.9	6.75; 1.88-24.2	
Likelihood ratio test (3 df)	. ,		39.18; <i>P</i> < 0.001	30.28; P < 0.001	
(trend, 1 df)			37.29; <i>P</i> < 0.001	28.28; <i>P</i> < 0.001	
Weight-for-age					
≥0	131 (20.2)	226 (34.8)	1.00	1.00	
-0.01 to -1	193 (29.7)	218 (33.5)	1.70; <i>1.26–2.30</i>	1.78; 1.30–2.44	
-1.01 to -2	197 (30.3)	144 (22.2)	3.20; 2.23-4.58	3.18; 2.19-4.64	
<-2	129 (19.8)	62 (9.5)	4.75; 3.12-7.23	4.57; 2.93-7.13	
Likelihood ratio test (3 df)	. ,	· · ·	72.52; P < 0.001	60.89; P < 0.001	
(trend, 1 df)			71.86; <i>P</i> < 0.001	60.10; <i>P</i> < 0.001	

* Based on the analysis of matched case-control sets.

^b Adjusted for income, education of the father and mother, and for any previous episode of pneumonia.

^c Figures in parentheses are percentages.

^d Figures in italics are the 95% confidence intervals.

ter of the control children had mothers who worked outside the home (associated odds ratio, 1.58; 95% CI = 1.21, 2.07). The risk of pneumonia increased with the proportion of time the mother had spent working since her child was born, e.g., from 1.21 when this proportion was <25% to 1.50 when this proportion was in the range 25–74%, and to 1.74 when the proportion was $\geq75\%$ (χ^2 test for trend = 4.63; P = 0.03).

Previous illnesses

The odds ratios associated with previous episodes of pneumonia and/or wheezing were high (see Table 1). Previous hospitalization for pneumonia was estimated to place a child at just over three times the risk of having a subsequent episode of pneumonia. Such hospitalization among young children is not uncommon, with 5.4% of the control children previously having been admitted for pneumonia.

There was also an increased risk of pneumonia among children who had previously suffered from episodes of wheezing, the risk increasing with the number of previous episodes. A child who had experienced three or more episodes of wheezing was almost four times (OR = 3.91) more likely to contract pneumonia than one who had never suffered

204

from wheezing. Although a relatively small proportion of the population was in this category (0.9% of control children) the magnitude of the risk factor is such that this association cannot be ignored.

Crowding

As in many previous studies, crowding appeared to increase the risk of childhood pneumonia in the study population. The risks increased with the total household size and the number of children at home. Statistically significant trends were observed for both these variables, with the odds ratio increasing to 1.99 for households with ≥ 8 persons, compared with the baseline category of 2–4 persons (χ^2 test for trend = 15.43; P < 0.001), and rising to 2.36 for children from families with ≥ 7 children, compared with the baseline category of 1–2 children (χ^2 test for trend = 7.52; P = 0.006). However, there was no association between the risk of pneumonia and the number of persons sleeping in the same room as the index child.

Mother's reproductive history

A high number of previous pregnancies was an important risk factor for pneumonia, with a strongly significant trend of increasing risk up to OR = 3.22

(95% CI: 1.66, 6.24) among children whose mothers had had \geq 7 pregnancies (χ^2 test for trend = 11.32; P < 0.001). In contrast, maternal age had a strong negative association, with the lowest risk (OR = 0.37) being found among children with mothers aged \geq 35 years (χ^2 test for trend = 10.79; P = 0.001).

Short birth interval, multiple births, and mothers who had had two or more abortions were all associated with an increased risk, but not significantly so. There was no evidence that antenatal care attendance, place and mode of delivery, previous stillbirths, or high birth order had an association with risk of pneumonia.

Exposure to smoke

Although the odds ratios for industrial smoke and passive smoking were moderately elevated, they were not statistically significant. There was also no evidence that indoor smoke arising from poor cooking facilities or lighting increased the risk of pneumonia.

Socioeconomic variables

The lack of association between any of the socioeconomic variables included in the study and risk of pneumonia may have been due to overmatching of these variables caused by the choice of neighbourhood controls, rather than because they did not affect the risk. The estimated odds ratios for lack of maternal education, poor quality housing, low income, and absence of piped water were remarkably close to unity. Although the risk associated with lack of paternal education was slightly raised, it was not significant since the 95% confidence interval (0.93, 1.98) included unity.

Vaccination status

Children who had completed their vaccination schedule for their age were 32% less likely to contract pneumonia than those who had not (95% CI: 12,48%). Statistically significant reductions of about 30% were observed for BCG, diphtheria-pertussistetanus (DPT) and poliovirus vaccines. Measles vaccine was associated with a nonsignificant 21% reduction in risk, which is consistent with the fact that children with measles-associated pneumonia were excluded from the study. These results may be a direct consequence of DPT vaccination, which would be expected to give some protection against childhood pneumonia. The association with poliovirus vaccination could have arisen because of the strong correlation between a child having or not having received the different vaccinations. Alterna-

Risk factors for childhood pneumonia in Brazil

tively, the observed reduction could have arisen because complete vaccination status acts as a marker for increased use of health services, better child-care practices or higher socioeconomic status. The last-mentioned is unlikely, however, in view of the lack of association between risk of pneumonia and more direct measures of socioeconomic status.

Discussion

Interpretation of our results requires several points to be borne in mind. For an individual child the magnitude of the odds ratio determines to what extent the child is at an increased risk if they have the risk factor. However, a combination of the magnitude of the odds ratio and the prevalence of the risk factor in the population determines to what extent the occurrence of pneumonia can be attributed to the risk factor. In terms of control, therefore, greater impact might be achieved by reducing the prevalence of a common risk factor with a modest odds ratio, e.g., an OR = 2, than by using interventions to control a rare risk factor with a higher associated risk, e.g., an OR = 6. In general, the larger the odds ratio, the more likely the observed association is to be causal rather than unaccountable confounding.

Malnutrition was the most important risk factor in our study population for the occurrence of cases of childhood pneumonia severe enough for a mother to take her child to hospital. The risk of pneumonia increased as the value of the Z-score decreased for all three anthropometric indices, with the odds ratios associated with the lowest categories of each index lying in the range 4.57-6.75.

Protein-calorie malnutrition resulting from an inadequate intake or utilization of calories or protein in the diet (8) is a major determinant of mortality risk in young children (9-11). The synergism between malnutrition and infectious diseases is well known. Protein and vitamin deficiency appear to inhibit formation of specific antibodies and also cause impairment of pulmonary defence mechanisms (12, 13).

An association between malnutrition and mortality from ARI has been suggested in various studies from developing countries. For example, in six South American cities one study reported that malnutrition was an associated cause of death in about 30-45% of the deaths from ARI among under-5year-olds (9); these results are noteworthy, despite the absence of a control group. Also, a study from Papua New Guinea reported that malnourished children (based on weight-for-age) had an eightfold higher risk of dying from acute lower respiratory

infections (ALRI) than well-nourished children (14); however, it is unclear whether adjustments were made for confounding. A population-based casecontrol study in Brazil of 127 infants who died from respiratory infections and who were matched with 254 neighbourhood controls reported that malnutrition (based on weight-for-age) was strongly associated with ARI mortality (OR = 21.5) (15). Finally, a recent longitudinal study of 492 children in Manila, Philippines, found that malnourished children were three times more likely than those who were well nourished to die from ALRI (16).

An association between malnutrition and pneumonia or ALRI case fatality rate has been reported in four hospital-based studies in which the children's nutritional status was determined on admission. In the Philippines, children whose weight-for-age Zscores were <-2 had a 20% case fatality rate for ALRI compared with 9.6% for those who were better nourished (16). In Papua New Guinea, the case fatality rate for severe pneumonia was twice as high among undernourished children (17). In Bangladesh, the case fatality rate for undernourished children with ALRI was reported to be 10%, while that for better nourished children was 6% (18). In Argentina, the ALRI case fatality rate was 7.6% among undernourished children and 2.3% among those who were well nourished (19). All of these studies indicate that nutritional status is an important determinant of pneumonia case fatality.

In a longitudinal study carried out in Brazil, undernourished children (based on weight-forheight) were about twice as likely to be hospitalized with pneumonia (20). Also, in a recent case-control study in Pôrto Alegre, Brazil, weight-for-age remained significantly associated with the risk of pneumonia after adjustment, with a fivefold increase for the most malnourished children (3).

Data have also been reported on the association between malnutrition (weight-for-age <10th percentile) and ALRI in four of the BOSTID studies (21). Children were divided into two age groups (0–17 months and 18–59 months). Only one study found that malnutrition was associated with ALRI (OR = 1.3) for the age group 0–17 months (24). For the age group \geq 18 months all four of the Board on Science and Technology for International Development (BOSTID) studies found an association between malnutrition and ALRI; the estimated relative risks lay in the range 1.2–2.7. No adjustment for confounding factors was carried out in any of these studies.

The data from the present study add support to the hypothesis that a reduction in the prevalence of protein-calorie malnutrition would have a substantial impact on pneumonia morbidity and mortality; it may also have additional effects on other causes of morbidity and mortality, most notably diarrhoea. The results lend weight to the recommendation made by Black & Sazawal that the feasibility and cost of interventions to reduce the prevalence of malnutrition should be examined and compared with other child survival interventions.^{*d*}

In view of the high prevalence of stunting in our study population (8.4% of control children had height-for-age Z-scores $\langle -3 \rangle$; and a cumulative 29.2% had Z-scores $\langle -2 \rangle$) there is an urgent need for local action in addition to the need to address the reduction of malnutrition as a global priority.

Increased risks were also observed for low birth weight (OR = 3.16 for children weighing <2000 g at birth) and for non-breast-feeding (OR = 1.69). The strengths of the associations were less than those with anthropometric indices. However, an OR = 3.16 for the occurrence of pneumonia later in life among children weighing <2000 g at birth cannot be ignored, particularly since low birth weight is associated with an extremely high risk of mortality in the neonatal period. Our study included only children who were older than this and who had therefore already passed safely through this danger period, and also because there is an association between low birth weight and increased diarrhoea morbidity and mortality.

It is also important to target non-breast-feeding. Although the estimated odds ratio was low, the prevalence of non-breast-feeding in the study population is high. Furthermore, studies from southern Brazil and elsewhere have demonstrated the strong protective effect of breast-feeding against infant mortality, with the effect being more marked for deaths caused by diarrhoea but also for deaths from pneumonia (15).

The second major finding to emerge from the study that deserves particular attention is the high odds ratio of childhood pneumonia that was associated with attendance at a day care centre. Although at present relatively few children in this poor urban area attend such centres, those who do have a greater than fivefold risk of contracting pneumonia (95% CI: 2.13,12.79). Our study is the first from a developing country to investigate this association. There has been one recent case-control study carried out in Atlanta, GA, USA, that reported an almost threefold increased risk of hospitalization for ALRI after controlling for several potential con-

^d Black RE, Sazawal. S. Interventions for the prevention of childhood pneumonia in developing countries: reducing the prevalence of mainutrition. Paper presented at a meeting of the International Expert Advisory Committee of WHO/ARI on Prevention of Childhood Pneumonia.

Risk factors for childhood pneumonia in Brazil

founding factors (22). Studies from developed countries have also demonstrated a link between attendance at day care centres and risk of acute upper respiratory infections (23).

The number of children enrolled in day care centres has increased dramatically in developed countries over the past 10 years. A similar increase is expected in developing countries, particularly among the urban poor, since more women are participating in the labour force to supplement family incomes. In our study, the mothers of approximately 80% of children attending a day care centre worked outside the home. In São Paulo, Brazil, approximately 10-20% of preschool children attend some day care facility. In Ceará State, where our study took place, the local government is committed to doubling the number of publicly funded day care centres over the next 3 years. In view of the magnitude of the odds ratios that we found in this study and of that reported by Victora et al. (3) in Pôrto Alegre, a prospective study is being carried out in Fortaleza by Fonseca et al. to confirm this observation and to exclude the possibility that it may be due to selection bias in the case-control studies, with those children in day care centres who become ill being more likely to be taken to hospital than those who stay at home. A parallel study is being conducted in Campinas by Barros et al. to compare disease rates in day care centres and to use the findings to improve the design of such centres and how they can be better managed to minimize the risk of pneumonia.

Finally, the increased risk of pneumonia experienced by children who have suffered previous episodes of wheezing or been hospitalized for pneumonia is noteworthy. This risk more than trebled when a child had previously been hospitalized for either pneumonia or for wheezing and was almost fourfold for children who had suffered three or more previous episodes of wheezing, irrespective of whether or not these required hospitalization. In our study 15.3% of children who presented with pneumonia had been admitted to hospital with at least one previous episode. Similar findings have been reported in a case-control study carried out recently in southern Brazil (3). To our knowledge, these are the first studies to examine the effect of a previous episode of pneumonia on the risk of a subsequent episode. The relationship between previous episodes of asthma, bronchitis and/or bronchiolitis, and respiratory illness has been investigated previously (24-26).

Our findings indicate that parents and health personnel should be made aware that children who have had a previous severe episode of wheezing or pneumonia and those suffering from repeated episodes of wheezing are at particularly high risk of contracting pneumonia. Also, parents should be given guidance on the need to seek early medical attention for any of their children who experience illnesses with respiratory symptoms. More generally, there is a need to assess the appropriateness of targeting this group of children with preventive interventions.

Acknowledgement

The study project was supported by the International Development Research Centre (IDRC), Canada, the Conselho Nacional de Desenvolvimento Cientifico e Tecnológico (CNPq), Brazil, and the United Kingdom Overseas Development Administration.

Résumé

Facteurs de risque de pneumonie infantile dans les quartiers pauvres de Fortaleza, Brésil: une étude cas-témoins

Cet article rapporte les résultats d'une étude castémoins réalisée entre juillet 1989 et juin 1990 à Fortaleza, dans l'Etat de Ceará (Brésil), pour déterminer les facteurs qui augmentent le risque de pneumonie infantile chez les habitants des taudis urbains. Les cas étaient 650 enfants de moins de deux ans ayant un diagnostic radiologique de pneumonie, recrutés sur une période d'une année civile dans le principal hôpital pédiatrique de la ville. Les témoins appariés selon l'âge ont été recrutés dans le voisinage du domicile des cas.

La comparaison entre les cas et les témoins a porté sur divers facteurs concernant les aspects socio-démographiques, l'environnement, la reproduction, la nutrition et la mortalité. Un questionnaire portant sur les facteurs de risque a en outre été remis à la mère de tous les cas et témoins ou à la personne ayant normalement la garde de l'enfant. Les questions ont été rédigées avec soin et les protocoles d'entretien ont été élaborés de façon à éviter les biais de mémorisation et les erreurs de classification des facteurs de risque. En particulier. pour les facteurs susceptibles d'être affectés par la présence de la maladie, comme l'allaitement au sein, les questions se rapportaient au dernier jour en bonne santé. Pour les témoins, les questions se rapportaient à la même date que pour le cas correspondant, afin d'éviter un biais de mémorisation. Les cas ont été pesés et mesurés à l'hôpital et les témoins à domicile.

La malnutrition était le plus important facteur de risque de pneumonie infantile dans la population

à l'étude, les autres facteurs importants étant les rapports poids/âge, taille/âge et poids/taille. Etant donné la forte prévalence du retard de croissance dans cette population, il est urgent de donner la priorité à la lutte contre la malnutrition.

Le recours à un centre de soins de jour était également associé à une valeur élevée de l'odds ratio. Comme le nombre d'enfants vus en consultation dans de tels centres est en augmentation aussi bien dans les pays en développement que dans les pays développés, il faudra améliorer la structure et la gestion de ces établissements en vue de réduire les risques de pneumonie.

On a également observé une association entre un risque accru de pneumonie infantile et le faible poids de naissance, l'absence d'allaitement au sein, le surpeuplement, la forte parité et une vaccination incomplète, mais non avec la situation socio-économique ni avec des variables environnementales. Enfin, chez les enfants ayant déjà souffert d'épisodes de sifflement respiratoire ou été hospitalisés pour une pneumonie, le risque de contracter une pneumonie était multiplié par trois.

References

- Childhood pneumonia: strategies to meet the challenge. In: Proceedings of the International Consultation on Acute Respiratory Infections, December 11–13 1991, Washington. London, Appropriate Health Resources and Technology Action Group, 1992.
- Miller D. Issues for the future of ARI control. In: Douglas RM, Kerby-Eaton E, eds. Acute respiratory infections in childhood: Proceedings of an International Workshop, Sydney, August 1984. Adelaide, University of Adelaide, 1985: 100–103.
- Victora CG et al. Risk factors for pneumonia among children in a Brazilian metropolitan area. *Pediatrics*, 1994, 93: 977–985.
- Schlesselman JJ. Case-control studies: design, conduct, analysis. New York, Oxford University Press, 1982.
- Kirkwood BR. Essentials of medical statistics. Oxford, Blackwell Scientific Publications, 1988.
- 6. Rothman KJ. Modern epidemiology. Boston, Little Brown & Co, 1986.
- Breslow NE, Day NE. Statistical methods in cancer research: the analysis of case-control studies. Lyon, International Agency for Research on Cancer, 1980 (IARC Scientific Publication No. 32).
- Brown KH, Solomons NW. Nutritional problems of developing countries. *Infectious disease clinics of North America*, 1991, 5: 297–317.
- 9. **Puffer RR, Serrano CV.** *Patterns of mortality in childhood.* Washington, Pan American Health Organization, 1973 (PAHO Scientific Publication 262).

- Chen LC, Chowdhury AKMA, Huffman SL. Anthropometric assessment of energy-protein malnutrition and subsequent risk of mortality among preschool children. *American journal of clinical nutrition*, 1980, 33: 1836–1845.
- Kielmann AA, McCord C. Weight-for-age as an index of risk of deaths in children. *Lancet*, 1978, 1: 1247–1250.
- Chandra RK. Nutrition and immunity: lessons from the past and new insights into the future. *American journal of clinical nutrition*, 1991, 53: 1087–1101.
- Neumann CG et al. Immunologic responses in malnourished children. American journal of clinical nutrition, 1975, 28: 89–104.
- Lehmann D, Howard P, Heywood P. Nutrition and morbidity: acute lower respiratory infection, diarrhoea and malaria. *Papua New Guinea medical journal*, 1988, 31: 109–116.
- Victora CG et al. Risk factors for deaths due to respiratory infections among Brazilian infants. *International journal of epidemiology*, 1989, 18: 918– 925.
- Tupasi TE et al. Malnutrition and acute respiratory infections in Filipino children. *Reviews of infectious diseases*, 1990, 12: S1047–S1054.
- Shann F, Barker J, Poore P. Clinical signs that predict death in children with severe pneumonia. *Pediatrics infectious diseases journal*, 1989, 8: 852–855.
- Rahman M et al. Acute lower respiratory infections in hospitalized patients with diarrhea in Dhaka, Bangladesh. *Reviews of infectious diseases*, 1990, 12: S899–S906.
- Weissenbacher M et al. Hospital-based study on acute respiratory tract infection in young children. *Reviews of infectious diseases*, 1990, 12: S889– S898.
- Victora CG et al. Pneumonia, diarrheas and growth in the first four years of life. A longitudinal study of 5914 urban Brazilian children. *American journal of clinical nutrition*, 1990, 52: 391–396.
- Selwyn BJ. The epidemiology of acute respiratory tract infection in young children: comparison of findings from several developing countries. *Reviews* of infectious diseases, 1990, 12: S870–S888.
- Anderson LJ et al. Day-care center attendance and hospitalization for lower respiratory tract illness. *Pediatrics*, 1988, 82: 300–308.
- Haskins R, Kotch J. Day care and illness: evidence, cost, and public policy. *Pediatrics*, 1986, 77: S951– S982.
- Mok JYQ, Simpson H. Outcome for acute bronchitis, bronchiolitis, and pneumonia in infancy. Archives of disease in childhood, 1984, 59: 306–309.
- Weiss ST et al. The relationship of respiratory infection in early childhood to the occurrence of increased level of bronchial responsiveness and atopy. *American review of respiratory diseases*, 1985, 131: 573– 578.
- Anderson HR et al. The natural history of asthma in childhood. *Journal of epidemiology and community health*, 1986, 40: 121–129.