PROTECTIVE AND RISK FACTORS FOR ACUTE RESPIRATORY INFECTIONS IN HOSPITALIZED URBAN MALAYSIAN CHILDREN: A CASE CONROL STUDY

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Abstract. We performed a case control study to examine protective and risk factors for acute respiratory infections (ARI) in hospitalized children in Kuala Lumpur. Consecutive children between the ages of one month and five years hospitalized for pneumonia (n = 143), acute bronchiolitis (n = 92), acute laryngotracheobronchitis (n = 32) and empyema (n = 4) were included as cases and were compared with 322 children hospitalized during the same 24 hour period for non-respiratory causes.

Potential risk and protective factors were initially analysed by univariate analysis. Logistic regression analysis confirmed that several home environmental factors were significantly associated with ARI. The presence of a coughing sibling (OR = 3.76, 95%CI 2.09, 6.77), a household with more than five members (OR = 1.52, 95%CI 1.03, 2.19) and sleeping with three other persons (OR = 1.45, 95%CI 1.00, 2.08) were independent risk factors. Significant host factors were history of allergy (OR = 2.50, 95%CI 1.74, 3.61) and ethnicity (Malay race) (OR = 2.07 95%CI, 1.27, 3.37). Breast feeding for at least one month was confirmed as an independent protective factor (OR = 0.58, 95%CI 0.38, 0.86). However, the study was not able to demonstrate that domestic air pollution had an adverse effect.

This study provides further evidence that home environmental factors, particularly those associated with crowding, may predispose to ARI and that breast feeding is an important protective factor.

INTRODUCTION

Acute respiratory infections (ARI) are a major cause of morbidity and mortality. In developing countries approximately 4.5 million children die each year of the problem, accounting for some 30% of childhood mortality (Berman, 1991). Pneumonia accounts for the majority of the deaths while measles, pertussis, bronchiolitis and croup are the other important causes.

Epidemiological studies have identified several risk factors for ARI, the most important being low birth weight (Datta *et al*, 1987; Lehmann *et al*, 1988), malnutrition (James, 1972; Tupasi *et al*, 1988), crowding (Ruutu *et al*, 1990; Selwyn, 1990), lack of breast feeding (Chandra, 1979), vitamin A deficiency (Sommer *et al*, 1984) domestic smoke (Sofolowe, 1968; Anderson, 1978), and parental smoking (Pedreira *et al*, 1985; Fergusson *et al*, 1980). Some of these risk factors require further corroborative evidence. For instance, the relative importance of crowding is still unclear (Berman, 1991). The effects of passive smoking and other indoor pollutants need to be examined in the tropical environment. Although breast feeding is accepted as a protective factor further evidence of its efficacy will strengthen previous studies that could have been confounded by many other environmental factors.

The relative importance of the risk factors depend on the populations studied. In relatively developed urban areas severe malnutrition may not be a prevalent condition but other factors such as lack of breast feeding, indoor air pollution and crowding may play some role in ARI morbidity and mortality. In this study we examined these risk factors in hospitalized children. We hypothesized that home environmental factors, such as domestic smoke, passive smoking and crowding were associated with and that breast feeding protected against ARI in children living in Kuala Lumpur.

MATERIALS AND METHODS

All children aged between one month and five years admitted to the pediatric wards of the

University Unit of the Kuala Lumpur General Hospital for ARI (pneumonia, acute bronchiolitis, acute infective stridor or empyema) between February 1989 end May 1990 inclusive were studied. Diagnoses were based on clinical and radiological criteria and were confirmed by the first two authors within 24 hours of admission. Pneumonia was diagnosed in children presenting with respiratory symptoms and radiological evidence of consolidation. Acute bronchiolitis was diagnosed in children less than six months old with respiratory symptoms who had clinical and radiological evidence of bronchiolitis as defined by Phelan *et al* (1990). Empyema was diagnosed in children with pneumonia who had radiological evidence of pleural effusion. Acute stridor was included if it was due to an infective cause as defined by the clinical syndromes of acute laryngotracheobronchitis, acute epiglottitis, posterior pharyngeal abscess and acute tracheitis (Phelan *et al*, 1990).

Children admitted during the same 24 hour period for non-respiratory causes were recruited as controls after matching for age. To avoid any misclassification of cases as controls children were excluded from being controls if their parents had a positive response to any of the following questions regarding respiratory symptoms and illnesses:

(a) Does your child cough even though he/she has no colds?

(b) Is your child chesty or does he/she often produce phlegm even though he/she has no colds?

(c) Does your child wheeze *ie* have a noise coming from the chest (and not just from the mouth, nose or throat) when he/she breathes?

(d) Has your child ever had shortness of breath associated with a wheeze?

(e) Has your child been hospitalized for a respiratory illness? and

(f) Has your child been diagnosed as an asthmatic by a doctor?

For both case and control groups children with the following underlying disorders were excluded: chronic and surgical conditions of the respiratory system, heart disease, acute and chronic renal failure, oncological disorders, tuberculosis, dengue hemorrhagic fever, immunological disorders, and gross malnutrition.

The parents of case and control children were interviewed by two trained research assistants using a standard questionnaire. The interviewers were not informed of the objectives and hypotheses of the study to avoid possible bias in the interviewing process. The questionnaire contained questions on demography and exposure to potential risk and protective factors.

As this study was focused on clinical syndromes of ARI expensive etiological investigations were not undertaken as part of the research. Etiological investigations were performed according to the needs of individual cases by the pediatricians in charge.

Statistical analysis was performed using the SAS statistical package. Analysis of categorical data were performed using the chi square statistic and the logistic regression. Odds ratios (OR) and their 95% confidence intervals (95% CI) were calculated. A statistical test result was considered significant if the p-value < 0.05.

RESULTS

The diagnoses of pneumonia, acute bronchiolitis, acute laryngotracheobronchitis and empyema were confirmed in 271 children (Table 1). Of these 155 were boys and 117 were girls. The ethnic distribution was 178 (65.7%) Malays, 52 (19.2%) Chinese and 41 (15.1%) Indians. As controls 322 children fulfilled the inclusion and exclusion criteria and were selected.

Table 1

Children hospitalized for ARI: diagnoses and age distributions.

Diagnoses	No.	Age (months) mean ± SD
Pneumonia	143	23.1 ± 27.6
Acute bronchiolitis	92	3.5 ± 1.6
Laryngotracheobronchitis	32	12.7 ± 7.1
Empyema	4	9.0 ± 7.9
All	271	15.1 ± 22.1

Table 2

Results of univariate analysis of risk factors for ARI in hospitalized children.

Factor	Prevalence (%)		OR (95% CI)	p
	Case (n = 271)	Control (n = 322)		
Age < 24 months	84.2	83.8	1.02 (0.66, 1.60)	NS
Male sex	56.9	57.0	1.00 (0.78, 1.51)	NS
Ethnic Malay	65.4	60.1	1.26 (0.90, 1.76)	NS
Father's education < 7 yr	25.0	23.7	1.08 (0.74, 1.57)	NS
Mother's education < 7 yr	34.6	32.7	1.09 (0.77, 1.53)	NS
Birth weight < 2.0 kg	14.0	10.6	1.37 (0.84, 2.25)	NS
Family history of asthma	22.1	12.8	1.93 (1.25, 2.99)	0.003
Previous diagnosed allergy	50.7	34.6	1.95 (1.40, 2.71)	0.000
Breast fed at least 1 month	57.7	66.0	0.70 (0.50, 0.98)	0.037
Coughing sibling(s)	20.7	6.9	3.54 (2.10, 5.97)	0.000
Crowding (home with > 5 persons)	55.5	41.7	1.74 (1.26, 2.40)	0.001
Wooden/semipermanent home	47.1	38.3	1.43 (1.03, 1.99)	0.032
Sleep with 3 others	57.0	43.9	1.69 (1.22, 2.34)	0.002
Paternal smoking	56.3	56.4	0.99 (0.72, 1.38)	NS
Firewood cooking fuel	8.1	6.9	1.20 (0.65, 2.21)	NS
Kerosene cooking fuel	13.6	14.6	0.92 (0.58, 1.46)	NS
Mosquito coil use at least 3 nights per week	45.2	46.4	0.95 (0.69, 1.32)	NS
Aerosol repellents use at least 3 nights per week	15.4	19.3	0.76 (0.50, 1.17)	NS

NS = not significant

Table 2 shows the variables that were determined by the questionnaire and the results of univariate analysis of these potential protective and risk factors. Several factors were found to be significantly associated with ARI. Host factors identified were family history of asthma and previous history of allergy. Significant environmental factors were presence of a coughing sibling, crowding (home with more than five persons), living in a wooden or semi-permanent house and sleeping with three other persons in a room. Breast feeding for at least one month was a significant protective factor. Indoor environmental factors such as passive smoking, exposure to firewood or kerosene stoves and exposure to mosquito repellents were not associated with hospitalization for ARI.

Logistic regression analysis was performed by including all the potential risk factors into the regression model without applying any stepwise procedure. The risk factors which remained significant in this analysis are shown in Table 3. Of the host factors only previous allergy remained significant.

Table 3

Results of multivariate analysis of risk factors for ARI in hospitalized children.

Factor	OR (95% CI)	p
Ethnic Malay	2.07 (1.27, 3.37)	0.0034
Previous allergy	2.50 (1.74, 3.61)	0.0000
Coughing sibling(s)	3.76 (2.09, 6.77)	0.0000
Crowding (home with > 5 persons)	1.52 (1.03, 2.19)	0.0258
Sleep with 3 others	1.45 (1.00, 2.08)	0.0484
Breast fed at least 1 month	0.58 (0.38, 0.86)	0.0072

* only significant factors are shown

However, ethnicity which was not a significant factor in the univariate analysis became significant after adjustment for other factors. Specifically, Malay children were significantly associated with increased

odds of hospitalization for ARI. The presence of a coughing sibling, crowding and sleeping with three other persons were the environmental factors that remained independently associated with hospitalization for ARI. Breast feeding for at least one month remained an independent protective factor.

DISCUSSION

We identified several risk factors associated with ARI among otherwise healthy hospitalized urban Malaysian children. These factors were ethnicity, previously diagnosed allergy, presence of coughing sibling(s), crowding in the household and crowding during sleep. In contrast, breast feeding for at least one month protected against ARI. However, this study was not able to show that indoor air pollution was associated with ARI.

The initial univariate analysis revealed the potential risk factors. Two of these, namely family history of asthma and living in a wooden or semi-permanent home, did not remain significant after multivariate analysis indicating the presence of confounding.

The results of the logistic regression analysis confirmed some of the findings of earlier studies. However, among the host factors the role of allergy is somewhat controversial. While earlier studies suggested an association with atopy some recent studies did not show any relationship (Cogswell *et al*, 1982; Isaacs *et al*, 1982). However, interest in the relationship is continuing. In our study we only determined allergy or atopy through a positive response to whether the child had been previously diagnosed by a doctor to be allergic to food, medications or pollen. This might not be a very sensitive way to determine allergy and bias may not be ruled out.

The social and physical environments contribute to increased incidence of ARI. Crowding has been shown in several studies to be associated with an increased risk for ARI. Several studies have indicated that crowding may be an important risk factor (Ruutu *et al*, 1990; Selwyn *et al*, 1990) but the evidence has not been unequivocal. The definition of crowding has varied from study to study and comparing results may be difficult. Thus the relative impact of crowding on ARI is still unclear (Berman, 1991). We examined crowding by defining it as the presence of more than five persons in the household and found that this was associated with increased odds for ARI. In addition to household crowding during sleep was examined as a separate variable. We found that sleeping with at least three other persons was an independent risk factor. Thus, a household with less than five individuals may still have a higher risk for ARI in a child if members are crowded together during sleep. These two findings taken together seem to indicate that living in close proximity with many other persons is more important than the type of housing itself in increasing the risk for ARI. We observed that in the univariate analysis the type of housing was a significant factor but the association did not persist in the logistic regression analysis suggesting that the association was confounded by other variables.

The presence of a coughing sibling was also an independent risk factor. The presence of older siblings increased the risk for bronchiolitis in a case control study (McConnochie and Roghman, 1986). Sibling who are infected are obvious sources of transmission of infection.

The increased odds for ARI in Malay children is not readily explained. Social and environmental factors not detected in this study could have contributed to the observed relationship.

Our results did not show that children exposed to indoor environmental pollutants from various source such as environmental tobacco smoke, cooking fuels, namely kerosene and wood, and mosquito repellents were more likely to get significant ARI. This should not be interpreted to mean that these factors are not associated with ARI morbidity since this study was confined to hospitalized children. Children who are hospitalized belong to an extreme end of the spectrum of severity of ARI and thus this study could only identify those factors that could contribute to more severe ARI. Indoor air pollution may still play an important role in ARI morbidity in the community. Studies using direct measures of indoor air pollution may be more helpful in demonstrating this effect.

With regard to passive smoking we could only study maternal smoking since none of the mothers admitted to smoking. In whatever way paternal smoking was analysed, whether using categorical response *ie* yes/no response, or quantitative response *ie* the number of cigarettes smoked, no association was found. However, exposure to passive smoking was not quantified by measuring plasma or urinary nicotine levels. Passive smoking has been linked with hospitalization for acute bronchiolitis in a

recent study in Australia that measured urinary nicotine in case and controls (Reese *et al*, 1992). A study by us did show that children hospitalized with respiratory illnesses had higher urinary nicotine levels than controls (Chew *et al*, 1993). A study in the community showed that school children in Kuala Lumpur who were exposed to passive smoking had higher odds for getting a chest illness that would keep them inactive for at least three days (Azizi and Henry, 1991).

The protective effect of breast feeding was confirmed by our study. Previous evidence for the importance of breast feeding has shown protective effects against both morbidity and mortality. However, some of these studies were complicated by confounding variables (Berman, 1991). Additional evidence should be welcomed to strengthen the promotion of breast feeding particularly among urban families in developing countries.

The design and conduct of this study took into account the potential for biases. To avoid misclassification bias cases were individually confirmed by two of the investigators to avoid including other respiratory conditions in the study. For example, in our experience, wheezing and asthma may easily be mistaken for pneumonia without careful history, physical examination and sometimes radiological assessment. We chose to diagnose acute bronchiolitis only in those under six months to minimise misclassifying asthma as ARI. Stridor in young children may be due to non-infective causes and a careful assessment was necessary to determine the diagnosis. The exclusion of children with underlying disorders that could predispose to respiratory infections allowed us to focus on otherwise healthy children. Controls were those without any form of significant respiratory illness during the hospitalization or previously. The list of questions for exclusion of controls was important to avoid misclassification of cases as controls. Also if asthmatic children were allowed to be recruited as controls a bias that would result in failure to show effects would arise since similar risk factors may be shared by asthma and ARI.

The cases reflected the current clinical pattern of admission for ARI in our unit. The most notable observation was that acute stridor was wholly due to acute laryngotarcheobronchitis. Acute epiglottitis, bacterial tracheitis and posterior pharyngeal abscess were not detected during the period of the study. These conditions have been relatively uncommon among urban children over the past several years.

In conclusion this study identified several host and environmental factors that were associated with ARI in hospitalized children in Kuala Lumpur. Further studies need to be performed to examine in greater detail the importance of some of the potential risk factors that did not show any effects in this study. The roles of indoor air pollutants and passive smoking in a tropical environment have to be researched further.

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REFERENCES

Anderson HR. Respiratory abnormalities in Papua New Guinea children: the effects of locality and domestic wood smoke pollution. *Int J Epidemiol* 1978; 7 : 63-72.

Azizi BHO, Henry RL. The effects of indoor environmental factors on respiratory illness in primary school children in Kuala Lumpur. *Int J Epidemiol* 1991; 20 : 144-50.

Berman S. Epidemiology of acute respiratory infections in children of developing countries. *Rev Infect Dis* 1991; 13 (suppl 6) : S454-62

Chandra RK. Prospective studies of the effect of breast feeding on incidence of breast feeding and allergy. *Acta Pediatr Scan* 1979; 68 : 691-4.

Chew YY, Ton SH, Azizi O, Noriah R. Urinary nicotine as a measure of tobacco smoke exposure in children with respiratory diseases. *Mal J Med Lab Sci* 1993; 10 (2) : 61-4.

Cogswell JJ, Halliday DF, Alexander JR. Respiratory infections in the first year of life in children at risk of developing atopy. *Br Med J* 1982; 284 : 1011-3.

Datta N, Kumar V, Kumar L, Singhi S. Application of case management to the control of acute respiratory infections in low birth weight infants: a feasibility study. *Bull WHO* 1987; 65 : 77-82.

Fergusson DM, Horwood LJ, Shannon FT. Parental smoking and respiratory illness in infancy. *Arch Dis Child* 1980; 55 : 358-61.

Isaacs D, Clarke JR, Tyrell DA, Valman HB. Selective

infection of lower respiratory tract by respiratory viruses in children with recurrent respiratory tract infection. *Br Med J* 1982; 284 : 1011-3.

James JW. Longitudinal study of the morbidity of diarrhoeal and respiratory infections in malnourished children. *Am J Clin Nutr* 1972; 25 : 690-94.

Lehmann D, Howard P, Heywood P. Nutrition and morbidity: acute lower respiratory tract infections, diarrhoea and malaria. *PNG Med J* 1988; 31 : 109-60.

McConnochie KM, Roghman KJ. Parental smoking, presence of older siblings and family history of asthma increase of bronchitis. *Am J Dis Child* 1986; 140 : 806-12.

Pedreira FA, Guadolo VL, Feroli EJ, Mella GW, Weiss IP. Involuntary smoking and incidence of respiratory illness during the first year of life. *Pediatrics* 1985; 75 : 594-7.

Phelan PD, Landau LI, Olinsky A. Respiratory illness in children, 3rd ed. Oxford; Blackwell Scientific Publications, 1990.

Reese AC, James IR, Landau LI, Le Souef PN. Relationship between urinary nicotine level and diagnosis in children admitted to hospital. *Am Rev Respir Dis* 1992; 146 : 66-70.

Ruutu P, Halonen P, Meurman O, *et al.* Viral lower respiratory tract infections in Filipino children. *J Infect Dis* 1990; 161 : 175-9.

Selwyn BJ. On behalf of the Coordinated Data Group of Bostid Researchers. 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.

Sofolowe GO. Smoke pollution in dwellings of infants with bronchopneumonia. *Arch Environ Health* 1968; 16 : 670-2.

Sommer A, Katz J, Tarwotjo I. Increased risk of respiratory disease and diarrhoea in children with preexisting mild vitamin A deficiency. *Am J Clin Nutr* 1984; 40 : 1090-5.

Tupasi TE, Velmonte MA, Sanvictores MEG, Watkins CJ, Leeder SR, Corkhill RT. The relationship between breast and bottle feeding and respiratory illness in the first year of life. *J Epidemiol Commun Health* 1979; 33 : 180-2.