BMC Public Health

Research article

Open Access

Crowding: risk factor or protective factor for lower respiratory disease in young children?

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Published: 03 June 2004

BMC Public Health 2004, **4**:19

Received: 23 January 2004

Accepted: 03 June 2004

This article is available from: http://www.biomedcentral.com/1471-2458/4/19

Abstract

Background: To study the effects of household crowding upon the respiratory health of young children living in the city of São Paulo, Brazil.

Methods: Case-control study with children aged from 2 to 59 months living within the boundaries of the city of São Paulo. Cases were children recruited from 5 public hospitals in central São Paulo with an acute episode of lower respiratory disease. Children were classified into the following diagnostic categories: acute bronchitis, acute bronchiolitis, pneumonia, asthma, post-bronchiolitis wheezing and wheezing of uncertain aetiology. One control, crudely matched to each case with regard to age (<2, 2 years old or more), was selected among healthy children living in the neighborhood of the case.

All buildings were surveyed for the presence of environmental contaminants, type of construction and building material. Plans of all homes, including measurements of floor area, height of walls, windows and solar orientation, was performed. Data were analysed using conditional logistic regression.

Results: A total of 313 pairs of children were studied. Over 70% of the cases had a primary or an associated diagnosis of a wheezing illness. Compared with controls, cases tended to live in smaller houses with less adequate sewage disposal. Cases and controls were similar with respect to the number of people and the number of children under five living in the household, as well the number of people sharing the child's bedroom.

After controlling for potential confounders, no evidence of an association between number of persons sharing the child's bedroom and lower respiratory disease was identified when all cases were compared with their controls. However, when two categories of cases were distinguished (infections, asthma) and each category compared separately with their controls, crowding appeared to be associated with a 60% reduction in the incidence of asthma but with 2 1/2-fold increase in the incidence of lower respiratory tract infections ($p = 0.001$).

Conclusion: Our findings suggest that household crowding places young children at risk of acute lower respiratory infection but may protect against asthma. This result is consistent with the hygiene hypothesis.

Background

In the mid-nineteenth century, the emergence of germ theory and the empirical evidence that the highest incidence of severe infectious disease in cities occurred where the population was most dense (per hectare or per dwelling) led to a public health movement in Britain and the first statutory controls on housing – The Artisans and Labourers Dwellings Act 1848 [1]. Focusing on health, the requirements were that all habitable rooms have an openable window, that the dwellings be connected with a sewer, and that an earth or water closet be provided for every two dwellings. Since then, standards for dwellings have evolved over time to meet the broader health and social requirements of modern life.

In 1988, recognising that housing-related health problems were still a matter of concern in Europe, the World Health Organization (WHO) published the 'Guidelines for Healthy Housing' [2]. These guidelines, aimed particularly at developing middle-income countries in Europe (as defined by the World Bank), were intended to define minimum standards for new housing and to be a guide for assessing the quality of existing housing.

In the developing world, where urbanisation has been rapid in recent years with a lack of intervention in the housing market, a large proportion of the population is still living in conditions similar in many aspects to those of the nineteenth century citizens of London. Overcrowding, inadequate arrangements for excreta and waste disposal, poor ventilation, dampness, and numerous other housing problems remain threats to the health of low-income groups.

In this paper we examine the effects of household crowding upon the respiratory health of young children living in the city of São Paulo, Southeast Brazil.

Methods

We performed a case-control study to investigate household environmental risk factors for lower respiratory diseases in pre-school children.

Recruitment of cases

Cases were recruited from children aged from 2 to 59 months presenting to the emergency paediatric departments of five public hospitals located in central São Paulo with acute lower respiratory disease. Cases were classified into one of six diagnostic categories using the following criteria:

Acute bronchitis: children with no previous diagnosis of asthma who presented with cough and sputum after an upper respiratory tract infection of less than 3 weeks duration and without wheezing.

Acute bronchiolitis: children less than two years old with a history of upper respiratory tract infection followed by cough, breathlessness, tachypnoea, wheezing, crepitations, and pulmonary hyperinflation on chest X-ray.

Pneumonia: children found to have pulmonary infiltrate on chest X-ray with a history and clinical findings compatible with pneumonia.

Asthma: children presenting with wheezing or coughing triggered by a viral upper respiratory tract infection, allergens, irritants, exercise, weather changes or emotional stress, and a history of at least 2 similar episodes in the past.

Post-bronchiolitis wheezing: children presenting with recurrent wheezing after an acute episode of bronchiolitis.

Wheezing of uncertain aetiology: children with their first or second episode of wheezing without other characteristic signs or symptoms.

For children presenting with two distinct lower respiratory tract diseases, a primary and a secondary (or associated) diagnosis were assigned. The primary diagnosis was that most immediately related to the main complaint.

To be eligible for inclusion in the study, children had to live within the boundaries of the city of São Paulo and have lived in the same house for the last six months. Children were excluded from the study if they presented to the hospital with a recent history of aspiration of a liquid or of a foreign body, if they had a diagnosis of tuberculosis, measles or pertussis, or if they presented with underlying conditions such as congenital or inherited diseases, cancer, neurologic or neuromuscular diseases, immunological diseases, or gastroesophageal reflux.

Recruitment of controls

One control, crudely matched to the case with regard to age (<2 years, 2 years or more), was selected from among healthy children living in the neighbourhood of the case.

Exclusion criteria for the controls included those which applied to the cases. Furthermore, children were not recruited as controls if they presented with current symptoms of lower respiratory disease or if they had a history of asthma or of recurrent episodes of wheezing or pneumonia or of chronic upper respiratory disease. In addition, only children whose mothers reported that they would attend a public hospital if they had acute lower respiratory disease were included in the study.

Data collection

All potential cases were screened immediately upon arrival at the emergency paediatric department. Children who satisfied the basic eligibility criteria for the study were thoroughly examined by a paediatrician.

Having identified the case's household, neighbourhood controls were recruited by a field worker who proceeded in a systematic way asking in each neighbouring household whether there was a child of the required age group. When such a child was identified, the field worker administered a questionnaire to the mother/carer to establish the child's eligibility. If the child did not fulfil the eligibility criteria, the field worker continued the search.

Indoor environmental conditions (i.e., presence of contaminants and micro-climate) were assessed in all the cases' and neighbourhood controls' households. Plans of all homes with measurements of floor area, height of the walls, window area, and solar orientation were made.

Mothers of cases and controls were interviewed by trained field workers using a standardised questionnaire to collect detailed information on family composition, family history of asthma or atopy, reproductive history, child care practices, feeding practices, nutritional status, immunisation, hospitalisation, housing conditions, sanitation, habits with respect to ventilation of the house, heating and cleaning practices, socio-economic conditions, and smoking. Perinatal variables and immunisation data were obtained from the maternity card and immunisation card or, if these cards were unavailable, by recall.

Analysis

We used the number of persons sleeping in the child's bedroom as the indicator of crowding.

The ventilation of the houses was measured by two ways: (1) a ventilation index was created by dividing the total window area (m^2) by the volume of the houses (m^3) and multiplying by 100; (2) the mothers were asked to rate the ventilation of their homes using the scale: very good, good, average, bad or very bad.

The analysis was conducted based on a conceptual model of the relationships between household crowding and other putative risk factors for lower respiratory disease in children [3]. Based on these relations, a sequence of models was developed using conditional logistic regression analyses [4]. The more distant determinants of the outcome of interest were entered first. The models progressively included the more proximal variables until exposure to household crowding was reached. Sex and age of the child were included in all models on *a priori* grounds.

Although the age of the children was roughly similar for each case-control pair, as a result of the sampling procedure, a finer age grading (2–5; 6–11; 12–23; 24–35; and 36–59 months) was used in the matched analyses to improve control of age.

Two criteria were used to select variables for the final multivariate model: (1) statistical significance (p-value ≤ 0.05) for selecting variables in the initial models or (2) a clear change in the estimate of the effect of household crowding produced by the other variables not selected in the first steps of the analysis.

Unadjusted and adjusted odds ratios and their 95% confidence intervals are presented. The statistical significance of variables in the models was assessed by the likelihood ratio test (LRT) [4].

We also grouped the cases into two groups (a) those with a primary diagnosis of lower respiratory tract infection without recurrent wheezing (children with acute bronchitis, acute bronchiolitis, or pneumonia); (b) those with asthma (with or without an associated lower respiratory tract infection).

We then looked for evidence that the association between household overcrowding and respiratory disease differed for the two groups of cases by including an appropriate interaction term in both final models. Children presenting with post-bronchiolitis wheezing (with or without an associated infectious respiratory disease) or only with wheezing of uncertain aetiology were excluded from these analyses.

Results

Four hundred and eleven cases and 347 neighbourhood controls were initially enrolled in this study. After investigation, 13 cases were excluded from the study because of gastroesophageal reflux, sickle cell disease and HIV positivity. Two cases could not be traced after recruitment because of a change of home address. Eleven neighbourhood controls for these cases were also excluded from the study. Thus, a total of 396 cases and 336 neighbourhood controls were available for inclusion in the analysis. Missing data for some variables resulted in 313 case-control pairs being analysed.

Over 70% of the cases had a primary or an associated diagnosis of a wheezing illness, i.e., asthma, post-bronchiolitis wheezing or wheezing of uncertain aetiology.

Table 1 shows the distribution of the cases and controls according to the type of housing, access to basic amenities and different measures of crowding. The proportion of cases living in shantytowns or squats (38%) was higher

Table 1: Type of housing and the basic infrastructure of the cases' (n = 396) and neighbourhood controls'(n = 336) houses

Items	Cases		Neighbourhood Controls	
	n	%	n	%
Type of housing				
Traditional	209	53	212	63
Flat	35	9	23	7
Favela	121	30	77	23
Cortiço	31	8	24	7
Electricity				
Yes	393	99	333	99
No	3	1	3	1
Water supply				
piped water	382	97	330	98
public tap	14	3	6	2
Sewerage system				
mains sewers / septic tank	282	71	255	76
Other	114	29	81	24
Toilet				
Family	274	69	260	77
shared / none	122	31	76	23
N° of residents / n° of rooms				
<1.00	40	10	45	13
1.00 – 1.49	134	34	126	38
1.50 – 2.49	108	27	98	29
≥2.50	113	29	67	20
N° of residents / n° of bedrooms				
<3.00	81	21	71	21
3.00–3.49	91	23	88	26
3.50–4.99	104	26	85	25
≥ 5.00	119	30	92	28
N° of persons in the child's bedroom				
≤2	33	8	28	8
3	121	31	119	36
≥4	242	61	189	56

than that of controls (30%, $p = 0.04$). Fourteen percent of cases and 6% of controls lived in houses not connected to mains sewers or to a septic tank and where there was no toilet or the toilet had to be shared with other family ($p < 0.01$).

Having 4 or more persons (including the child under study) sharing the child's bedroom was slightly more frequent among cases (61%) than controls (56%), but this difference was not statistically significant ($p = 0.27$). No difference was found when the proportion of cases sharing their beds (57%) was compared with that of controls (53%; $p = 0.45$).

There was no difference between the mean value of the index of ventilation of the cases' houses (3.08 m^2/m^3) and controls' houses (3.14 m^2/m^3; paired t-test: $p = 0.47$). However, mothers of controls tended to report good or very good ventilation more frequently than the cases' mothers (48% versus 39%, $p = 0.01$)

The mean floor area of the cases' houses (31.9 m^2) was smaller than that of controls' (34.7 m^2, paired t-test: $p = 0.02$).

The mean number of residents in cases' households (5.12 persons) was similar to the mean number of residents in controls' households (5.07 persons, $p = 0.98$). No difference was observed between the mean numbers of under-fives in the households when cases were compared with neighbourhood controls ($p = 0.56$).

Table 2 presents the results of the unadjusted and adjusted analyses of the association between number of persons sharing the child's bedroom and lower respiratory disease in children. There was no evidence of an association between number of persons sharing the child's bedroom

Table 2: Unadjusted and adjusted odds ratios (OR)*, confidence intervals (95% CI) and *p*-values for number of persons sharing the child's bedroom when all cases of lower respiratory disease were compared with neighbourhood controls.

Variables	Unadjusted OR (95% CI)	Adjusted OR * (95% CI)
No. of persons sharing the child's bedroom		
< 4	1.00	1.00
≥4	1.17 (0.85–1.61)	1.09 (0.73–1.63)
LRT (1 df)	$p = 0.33$	$p = 0.66$

* adjusted for sex, age, immunisation status, current breast-feeding, attendance at crèche, family history of asthma or atopy, ventilation rated by child's mother, income per capita, house ownership, social class, and adequate sanitary arrangements

Table 3: Adjusted odds ratios (OR) and confidence intervals (95% CI) for number of persons sharing the child's bedroom for cases of asthma and cases of infection compared with neighbourhood controls.

	NEIGHBOURHOOD CONTROLS No. of persons sharing the child's bedroom *		
	< 4	≥4	OR** (95% CI)
ASTHMA CASES			
No. of persons sharing the child's bedroom *			
< 4	23	39	1.00
≥4	29	41	0.42 (0.21–0.87)
CASES OF INFECTION			
No. of persons sharing the child's bedroom *			
< 4	15	13	1.00
≥4	30	28	2.50 (1.02–6.09)

* number of case-control pairs ** adjusted for the same variables presented in Table 2 LRT: $p = 0.001$

and lower respiratory disease as a whole when all cases were compared with the neighbourhood control group (OR = 1.09, 95%CI: 0.73–1.63; $p = 0.66$).

There was however, strong evidence that the association between crowding and lower respiratory disease depends on the nature of the disease – infectious or non-infectious (($p = 0.001$), Table 3). Crowding was associated with a 60% reduction in the incidence of asthma but with 2 1/2-fold increase in the incidence of lower respiratory tract infections.

Discussion

Our data suggest that while household crowding places young children at increased risk of acute lower respiratory infection, it may protect against asthma. Failure to distinguish cases of lower respiratory disease due to infection from those of non-infectious aetiology (asthma) results in an apparent lack of association between crowding and lower respiratory disease because the two opposing effects cancel each other out.

Our study sample comprised mainly by low-income families living in rather small houses. WHO guidelines [2] recommend 12 m^2 of habitable space per person. On average each person in our study families had 7 m^2 available in their homes (cases, 6.8 m^2 and neighbourhood controls, 7.3 m^2). Only 12% of the families were living in households which met the WHO recommendation (cases, 12.2% and neighbourhood controls, 12.5%). We chose the number of persons sleeping in the child's bedroom as the indicator for crowding because we believed that this variable reflects an important aspect of crowding. We repeated the same analyses with the other measures of crowding (always using as cutoff point the median value) and similar results were observed (data not shown).

Our cases were diagnosed in hospital settings by experienced paediatricians using a standardised diagnostic criteria (further discussion on the diagnostic criteria used in this study is presented elsewhere [5]) and our estimates were controlled for important confounders for both respiratory infections and asthma. It is worth noting that the effect of crowding that we found was independent of the level of ventilation of the house, which was subjectively and objectively measured in our study. The results presented are those obtained when the mother's opinion of ventilation was included in the multivariate model, but similar results were obtained when using our ventilation index (data not shown).

In addition, the inclusion of attendance at crèche in the models will have controlled to a degree the influence of other crowded indoor spaces in which the children may spend considerable part of the day.

Crowding may plausibly increase the risk of respiratory infection by increasing the opportunity for cross infection among the family. The agents of such infections are readily transmitted, usually through air by droplets or aerosols, in crowded and ill-ventilated rooms where people are sneezing, coughing or simply talking [2]. A number of epidemiological studies, using different measures of crowding such as total number of residents in the home, number of siblings, number of persons sharing the bed, room occupancy, and population density, have reported an association between crowding and respiratory diseases [6-11].

Two case-control studies conducted in South America reported an association between household crowding and increased incidence of acute lower respiratory infection in young children [7,9]. Using three indicators of crowding, Cerqueiro et al. [7] reported for inpatients odds ratios of the order of two associated with living in a household with more than 2 persons per room, with more than 4 siblings, and bed sharing. For outpatients, only the association between lower respiratory infection and number of siblings was statistically significant. Victora et al. [9] reported that the incidence of pneumonia increased as the number of persons in the household increased. Compared with households with 2–3 persons, the odds ratio associated with living in a household with 4–5 persons was 1.54 (95%CI: 1.07–2.20) and for households with 6 or more persons was 1.84 (95%CI: 1.24–2.74), after controlling for socio-economic conditions of the families.

A one year follow-up study of the association between household crowding and acute lower respiratory infections among young Kenyan children [10] found that children with more than 5 siblings living in the household were at increased risk of disease (RR = 3.2 and 95%CI: 1.2–8.5 adjusted for geographic region). No association was observed in this study when crowding was measured by the number of children sharing a bed.

Crowding was also identified as an important determinant of infant mortality due to respiratory infections in two case-control studies carried out in Brazil. Victora et al. [6] compared infants who died from a respiratory infection with neighbourhood controls. These authors reported statistically significant associations between both the number of people per bedroom and the number of under-fives in the family and mortality, after adjusting for employment status, income and education of the parents. Niobey et al. [8], comparing infants who died from pneumonia with neighbourhood controls in the metropolitan region of the Rio de Janeiro, found an odds ratio of 2.67 (95%CI: 1.83–3.88) for living in a household with 5 or more persons. This estimate was adjusted for birth weight, immunisation by BCG and age at weaning.

In a more recent study Parker et al. [11], reanalysing old data from a cohort of infants born in 1947, reported a relative risk of 1.29 (95%CI: 1.02–1.62) for severe respiratory infection for children living in overcrowded houses (>2 persons in a one room dwelling, 3 in two rooms, 5 in three rooms, 8 or more in 4 rooms and more than 2 persons per room in houses of five rooms or more), after controlling for social class.

In contrast with the studies described above, some authors have reported a protective effect of crowding on the incidence of atopy and of non-infectious respiratory diseases. Strachan [12], after finding that hay fever and eczema were inversely related to the number of children in the household in a national sample of 17,414 British children, advanced the hypothesis that allergic diseases might be prevented by viral infections in early childhood, particularly those of the respiratory tract, transmitted by older siblings or acquired prenatally from a mother infected by her older children.

Other studies support this theory. Golding & Peters [13] analysed the 1970 UK national birth cohort data and reported that the proportion of children with hay fever by 5 years of age decreased with the number of older children in the house. Von Mutius et al. [14], in a cross-sectional survey of atopy among schoolchildren in Germany, found a significant inverse relation between the total number of siblings and prevalence of atopy (measured by skin prick test) after adjusting for several variables. A study from Sweden, Poland and Estonia reported similar findings [15]. The risk of atopic sensitisation was found to decrease at all study sites with increasing number of persons per room.

Two studies have reported a relationship between birth order and wheeze or asthma. Over 20 thousand Israeli army recruits participated in a study of risk factors for developing asthma by the age of 17 years [16]. A statistically significant association between birth order and asthma was observed, however this relationship was non-linear. Second-born recruits were more likely to have asthma compared with first-born recruits, with decreasing risk then observed for third/fourth and subsequently born recruits compared with second-born persons. In New Zealand, a study conducted among school-children [17] found an inverse relationship between the number of older children in the household and prevalence of wheezing, decreasing from 25% among first-born children to 6.7% among those with three or more older siblings. Nevertheless, no adjusted analysis was reported.

Case-control studies aiming at investigating the association between asthma and crowding proxy variables in early childhood have shown similar results. In Montreal, a study [18] with 457 children aged 3–4 years with a diagnosis of asthma and 457 controls matched by age estimated, after adjusting for confounding variables, that the odds ratio for living with one sibling was 0.54 (95%CI: 0.36–0.80) and 0.49 (95%CI: 0.30–0.81) for living with more than one sibling, when comparing with children with none. The authors also reported a protective effect of day care attendance before 1 year of age (OR = 0.59; 95%CI: 040–0.87), compared with no day care attendance.

Another case-control study in New Zealand [19], after controlling for confounders (infections, atopy, socio-economic status), reported a strong association between asthma in childhood and family size. The estimated odds ratios for having no sibling and one sibling compared with having two or more siblings were 2.51 (95%CI: 1.05–6.01) and 1.86 (95%CI: 1.14–3.03), respectively. In this study day care attendance in the first year of life was not associated with asthma.

An interesting study conducted among 240 atopic (including respiratory allergy) and 240 non-atopic Italian military cadets used serology for food borne and faecal oral infections, such as *Toxoplasma gondii*, hepatitis A virus and *Helicobacter pylori*, as markers of levels of infection in childhood [20]. Atopy was reported to be less frequent among persons with positive serology. After adjusting for siblings' age, parental education and population density, the odds ratio was 0.7 for one exposure and 0.37 for two or more exposures ($p < 0.0001$), when compared with exposure to none of these antigens. Allergic asthma was rare (0.4%) among the participants exposed to at least two of the infections cited above.

Very few studies on asthma and crowding have been conducted in less developed countries. A cross-sectional study of 5,642 Bangladesh people aiming at estimating the prevalence and risk factors for asthma reported a higher prevalence of asthma among children living in households with 3 or less persons than in larger households (OR = 1.41; 95%CI: 1.01–1.92) [21].

All these studies concluded that exposure to air- or food-borne infections at early ages might protect against respiratory allergy and suggest that reduced exposure to such infections might have a role in recent increases in the prevalence of allergies in the developed countries.

Some studies, however, have failed to demonstrate an inverse association between crowding and non-infectious respiratory symptoms or disease. Martinez and colleagues [22] investigated, in a prospective study, risk factors for wheezing lower respiratory diseases in the first year of life. An increasing risk of these diseases was observed with increasing birth order. After adjusting for a number of confounders, odds ratios for illness increased to 2.2 (95%CI: 1.5–3.3) for fourth- or subsequently-born children compared to first-born children. These authors published more recently a subsequent study performed among the same children when they were 6 years old [23]. In this latter paper, the authors report that many of the infants with wheezing had transient conditions, due to viral infections, not related with increased risk of asthma or allergies later in life. Thus, this may partly explain the results obtained in the analysis of birth order.

Arguing that only indirect evidence (by crowding) exists that infection in early childhood may be protective for allergic diseases, Shaheen and colleagues [24] conducted a historical cohort study in Guinea-Bissau to investigate whether measles infection protects against the development of atopy in children. Young adults (14–21 years) with a history of measles infection recorded in childhood (0–6 years) were compared with those without such a history with regard to atopy (skin test positivity). Measles infection was found to be associated with a substantial reduction in the risk of atopy (OR = 0.36, 95%CI: 0.17–0.78) after adjustment for age, sex, month of test, mother's schooling, breastfeeding, and pigs kept in house.

The immunological basis of the hygiene theory is that the pattern of immune response *in utero* and in young children is different from that in older children and adults. The immune response of the former is based on a preponderance of cytokines of the T-helper 2 type (Th-2) with production of interleukins 5, 9, 13, whereas in adults it is based on Th-1 type immunoresponse which is self-limited and leads to low levels of IgE. The type 2 response tends to increase IgE, eosinophily and hyper-reactivity of the respiratory tract [25]. It is believed that microbial infections in early childhood lead to earlier maturation of the immune response and a shift from the Th2 to a Th1 type pattern, resulting in less frequent atopic responses.

Conclusion

Our results are in accord with the findings of the majority of the previous studies described above and are consistent with the hygiene hypothesis. This theory proposes that reduction of stimulation by microrganisms in the environment, as a result of improvements in public health and hygiene, may have influenced the immunoresponse in early childhood resulting in an increased predisposition to allergic diseases. This could partially explain the increase in these diseases in the last decades in some countries.

List of Abbreviations

CI: confidence interval

LRT: likelihood ratio test

OR: odds ratio

RR: relative risk

WHO: World Health Organization

Competing interests

None declared.

Authors' contributions

MRAC: principal investigator, conceived and designed the study, performed analyses, interpretation of results and drafted the manuscript. SNC: helped in the study design, statistical analysis, interpretation of results and contributed to manuscript writing. LFGS: responsible for environmental measurements and contributed to manuscript writing. FMA: chest physician responsible for the children's diagnosis. LAVD: contributed to manuscript writing. All authors read and approved the final manuscript.

Acknowledgements

This research was funded by the International Development Research Centre (IDRC) – Canada. The authors were supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) – Brazil[1], Overseas Research Scheme – United Kingdom[1] and Overseas Development Administration – United Kingdom[2]

The authors wish to express their enormous gratitude and respect to the families and children who participated in this study. Without their generosity this work would not have been possible.

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Pre-publication history

The pre-publication history for this paper can be accessed here:

http://www.biomedcentral.com/1471-2458/4/19/prepub