Eur J Pediatr (2013) 172:493–499
DOI 10.1007/s00431-012-1909-z

ORIGINAL ARTICLE

Factors associated with community-acquired pneumonia in hospitalised children and adolescents aged 6 months to 13 years old

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Received: 3 September 2012 / Revised: 27 November 2012 / Accepted: 29 November 2012 / Published online: 28 December 2012

Abstract According to the World Health Organisation, community-acquired pneumonia is the main cause of paediatric death, accounting for 20 % of deaths in children younger than 5 years old, and 90 % of these deaths occur in non-industrialised countries. This study has as objective to evaluate the influence of socio-economic, environmental and breastfeeding factors on the occurrence of pneumonia. An unmatched case–control study was conducted in children aged 6 months to 13 years old at a children's hospital in Brazil. Multivariate analysis by logistic regression was performed to determine the variables used to predict pneumonia. A total of 252 children were selected. In the adjusted (by age) multivariate analysis, the following variables were associated with community-acquired pneumonia: (a) protective factors: breastfeeding >3 months, absence of other unrelated comorbidities, non-smoking mother, being the only child, child's age >5 years and mother's age >19 years old; (b) risk factors: maternal education <8 years and child's birth order [≥second]. In the multivariate analysis, considering only children from 6 months to 5 years old, the following variables were associated with community-acquired pneumonia: (a) protective factors: breastfeeding >3 months, non-smoking mother and no smokers in the child's bedroom; (b) risk factors: maternal education <8 years and prenatal complications. *Conclusion*: These findings contribute favourably to effectively minimising the risk factors related to the disease process and natural history of community-acquired pneumonia.

Keywords Community-acquired pneumonia · Children · Hospitalisation · Case–control study

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Introduction

Community-acquired pneumonia (CAP) is a disease of the lower respiratory tract in which alveoli [12, 23] are affected. According to the World Health Organisation (WHO), CAP is the main cause of paediatric death, accounting for 20 % of deaths in children younger than 5 years old [26]; the incidence tends to increase in this population every year [5]. In addition, WHO reports show that 90 % of these deaths occur in non-industrialised countries [30, 31].

The increase in the risk of CAP has been associated with several factors [10, 13], which may be inherent to the individual (host) or the environment (in the broadest sense). Socio-economic status, age, low birth weight, duration of breastfeeding, malnutrition, lack of micronutrients, previous respiratory infections [9] and primary diseases are some of the main factors directly related to the individual. Among the main environmental factors, one can highlight passive smoking, dense population and living in urban areas with high levels of air pollution. The main factors related to the individual's socio-economic status include poor housing and sanitation conditions, difficult access to health care services, incomplete vaccination, low per capita income and low education level of

the parents [7, 17, 19, 20]. In non-industrialised countries, CAP is a serious public health problem, demanding efficient strategies to identify risk factors in order to develop effective interventions [17]. The objective of the present study was to evaluate the influence of socio-economic, environmental factors and breastfeeding on the prevalence of CAP in children aged over 6 months old who were hospitalised.

Methods

An unmatched case–control study was conducted (from October 2010 to April 2011) at the Philanthropic Children's Hospital in Uberaba, Minas Gerais State, Brazil.

Definition of cases and controls

Inclusion criteria for cases and controls

The cases were children and adolescents 6 months to 13 years old. Cases were consecutively selected hospitalised patients with indications of CAP confirmed by physical examination plus history based on WHO criteria [26, 31]: clinical, i.e., fever (axillary temperature ≥38,8 °C) and tachypnoea (according to the patient's age) plus chest indrawing; laboratory, i.e., WBC count ≥15,000/mm^3 [1] with polymorphonuclear leukocytes higher than 70 % and band count ≥500/mm^3 [1] and C-reactive protein >40 mg/l [1]; anterior–posterior chest X-ray (based on analysis of an experienced radiologist, only radiologically confirmed CAP cases, i.e., the presence of the pulmonary infiltrates that were well-defined and involved the mid- or peripheral portions of the lung lobe, pleural effusions and abscess or pneumatocele formation, were included).

Controls consisted of children and adolescents who were diagnosed with non-infectious and other infectious diseases, without CAP (absence of changes upon physical examination plus history, with normal chest X-ray), and were being admitted to the same hospital for treatment of the disease in question, clinical observation and propaedeutic exams.

Exclusion criteria for cases and controls

Children younger than 6 months old and older than 13 years old, or who presented some comorbidities such as chronic respiratory (asthma, bronchitis, bronchopulmonary dysplasia) cardiovascular (congenital heart disease, congestive heart failure, myocarditis) or neurological (cerebral palsy, neuromuscular respiratory disease, refractory epilepsy) diseases were not included. In addition, children with incomplete follow-up, or who developed complications during the study which might influence screening or analysis, or cases or controls with poor data were all excluded as well.

Data collection

Data were collected by means of a structured questionnaire applied by physicians to the child's mother during hospitalisation. The questionnaire consisted of: (a) the child's characteristics, (b) maternal and gestational characteristics and (c) socio-economic and environmental characteristics

Sample size and statistical analysis

Sample size was calculated considering that the incidence of CAP is approximately 0.29/1,000 in non-industrialised countries, including the prevalence of risk factors known to cause pneumonia, which is approximately 66 % among children with CAP, and the prevalence of breastfeeding, which is less than 50 % in children without the disease. Therefore, considering that an estimate of association (OR) of 2.0 between the main explicative variables and the response variable is frequently seen in most studies on the topic, it was necessary to select 110 children for each group at a ratio of 1:1. To verify the associations between variables, the odds ratio was used with a 95 % confidence interval, by means of multivariate logistic regression analysis (with adjustments), considering potentially bias-inducing variables. To verify the differences between measures of central tendency, Student's *t* test and the Kruskal–Wallis test were used for independent samples. The difference between proportions was verified using the chi-squared test (x^2), and the level of significance was set at 5 % for all analyses. The statistical package SPPS 20.0™ was employed for storage and analysis of data. The study was approved by the Research Ethics Committee of the Ribeirão Preto School of Medicine (413/CEP-CSE-FMRP-USP).

Results

A total of 252 children were selected for the study, with 126 in the case group and 126 in the control group. With regard to the demographic characteristics, male children were predominant in the case group (53.9 %), although the total sample was 49.6 % male ($p>0.05$).

By comparing the mean and median values of the continuous variables between both groups and considering children and adolescents from 6 months to 13 years old, one can observe that the cases showed lower age mean and haemoglobin count mean, as well as leukocytosis with neutrophilia, tachypnoea and higher level of reactive C protein (RCP) (Table 1), with significant differences ($p<0.05$).

Table 1 Distribution and comparison of mean values and its 95 % CI of the variables between cases and controls, considering children and adolescents from 6 months to 13 years old

	Cases mean (±SD)	(95 % CI)	Controls mean (±SD)	(95 % CI)
Birth weight (kg)	3.2 (0.5)	(3.1–3.3)	3.3 (0.4)	(3.2–3.4)
Age (months)[a]	32.2 (28.2)	(27.2–37.2)	63.4 (44.6)	(55.5–71.2)
Symptom duration[b] (days)	4.1 (3.7)	(3.4–4.7)	3.9 (5.8)	(2.9–5.0)
RR (irpm)[a]	42 (12.6)	(39.6–44.0)	27 (10.4)	(25.4–29.1)
Number of people at home	4.4 (1.6)	(4.1–4.7)	4.1 (1.4)	(3.8–4.3)
People per room	2.5 (1.0)	(2.3–2.7)	2.2 (0.9)	(2.0–2.4)
Number of rooms	4.6 (1.5)	(4.3–4.9)	4.8 (1.6)	(4.5–5.1)
Haemoglobins g/%[a]	10.8 (1.4)	(10.5–11.1)	11.8 (2.5)	(11.3–11.9)
Red blood cell s/mm^3	4.47 (0.5)	(4.3–4.5)	4.35 (0.5)	(4.26–4.44)
White blood cells/mm^{3a}	16,555 (8,303)	(15,000–18,000)	12,838 (6,228)	(11,740–13,930)
Band cells (%)[a]	10.8 (7.73)	(9.3–12.4)	4.9 (4.18)	(3.7–6.00)
Segmented cells (%)	55 (15.3)	(52.4–57.8)	52 (16.4)	(48.8–54.6)
Lymphocytes (%)	25 (13.7)	(22.8–29.5)	32 (16.5)	(29.5–35.3)
RCP (mg/dl)[a]	78 (56.3)	(67.2–89.1)	46 (48.7)	(33.4–58.0)
Mother's age[b]	27.7 (6.7)	(26.5–28.9)	29.7 (7.0)	(28.5–30.9)
Pregnancies[b]	2.6 (1.5)	(2.2–2.8)	2.2 (1.2)	(1.9–2.4)

RR respiratory rate, *RCP* reactive C protein

[a]Differences in mean and median values

[b]Statistical different in mean values but no difference in the median values

Considering only among children aged 6 months to 5 years old, the differences ($p<0.05$) were that the cases showed lower age mean and haemoglobin count mean, greater total leukocyte count with neutrophilia and higher level of RCP and tachypnoea (Table 2).

When adjusted (by age), multivariate analysis of the associations between variables (Table 3) showed that a duration of breastfeeding over 3 months, absence of comorbidities (other than those reported in the exclusion criteria), being the child of a non-smoking mother, being a single child, the absence of smokers in the child's bedroom and mother's age >19 years old were significant clinical factors preventing the development of pneumonia. The mother's level of education <8 years and being born >second were the variables found to be associated with the development of pneumonia and hospitalisation (potential risk factors).

Multivariate analysis of the associations between variables (Table 4), considering only children from 6 months to 5 years old, showed that a duration of breastfeeding over 3 months, being the child of a non-smoking mother, and the

Table 2 Distribution and comparison of mean values and its 95 % CI of the variables between cases and controls, considering children from 6 months to 5 years old

	Cases (*N*=113) mean (±SD)	(95 % CI)	Controls (*N*=74) mean (±SD)	(95 % CI)
Birth weight (kg)	3.1 (0.5)	(3.0–3.25)	3.2 (0.5)	(3.1–3.4)
Age (months)[a]	24.8 (14.7)	(27.2–37.2)	30.2 (44.6)	(26.5–33.8)
Symptom duration[b] (days)	4.1 (3.8)	(3.4–4.8)	3.7 (5.7)	(2.4–5.0)
RR (irpm)[a]	43.5 (12.6)	(41.2–45.7)	32.4 (10.4)	(30.1–34.8)
Number of people at home	4.5 (1.5)	(4.2–4.8)	4.1 (1.6)	(3.7–4.5)
People per room	2.5 (1.0)	(2.3–2.7)	2.4 (0.9)	(2.2–2.7)
Number of rooms	4.5 (1.5)	(4.3–4.8)	4.6 (1.3)	(4.3–4.9)
Haemoglobins g/%[a]	10.6 (1.4)	(10.4–10.9)	11.1 (1.0)	(10.8–11.3)
Red blood cell s/mm^3	4.44 (0.4)	(4.3–4.5)	4.22 (0.5)	(4.11–4.33)
White blood cells/mm^{3a}	16,128 (8,005)	(15,000–18,000)	13,735 (7,072)	(12,096–15,373)
Band cells (%)[a]	10.75 (8.8)	(9.1–12.4)	5.5 (6.8)	(3.9–7.10)
Segmented cells (%)[a]	53.4 (15.1)	(50.6–56.2)	48.8 (14.9)	(45.4–52.3)
Lymphocytes (%)	26.7 (13.5)	(24.2–29.3)	34.8 (16.4)	(31.0–38.6)
RCP (mg/dl)[a]	75.5 (56.4)	(63.9–87.0)	53 (50.3)	(36.9–69.1)
Mother's age[b]	27.2 (6.5)	(26.0–28.4)	27.1 (5.9)	(25.7–28.4)
Pregnancies	2.5 (1.5)	(2.26–2.85)	2.1 (1.3)	(1.8–2.4)

RR respiratory rate, *RCP* reactive C protein

[a]Differences in mean and median values

[b]Statistical difference in mean values but no difference in the median values

Table 3 Associations between independent variables and response variable (pneumonia) through multivariate logistic regression analysis, using crude and adjusted (by age) odds ratio

Variables	OR (crude)	95 % CI	OR (adjusted by age)	95 % CI
Breastfeeding (>3 months)[a]	0.14	0.06–0.30	0.18	0.09–0.36[a]
Absence of comorbidities[a]	0.26	0.07–0.90	0.32	0.10–0.90[a]
Complications	0.21	0.03–1.40	0.25	0.04–1.33
Colour (ethnics)—White	0.95	0.44–2.00	0.93	0.40–1.95
Father's educational level (<8 years)	1.05	0.44–2.50	1.18	0.56–2.50
Mother's educational level (<8 years)[a]	2.50	1.10–6.00[a]	2.29	1.07–4.86[a]
Non-smoking mother[a]	0.20	0.07–0.50[a]	0.19	0.08–0.45[a]
Non-smoking father	0.70	0.28–1.79	1.00	0.44–2.25
Single child[a]	0.43	0.20–0.89[a]	0.49	0.30–0.82[a]
Maternal weight gain (>10 kg)	1.35	0.61–2.90	1.08	0.53–2.2
House with water supply	4.00	0.07–23.5	5.70	0.13–24.3
House with basic sanitation	0.02	0.004–1.80	0.06	0.01–3.18
People in the house (≥2)	1.09	0.78–1.51	1.00	0.65–1.31
People in the bedroom (≥1)	1.31	0.86–2.00	1.06	0.80–1.82
Age >5 years[a]	0.21	0.07–0.60[a]	–	–
Mother's age (>19 years)	0.95	0.89–1.02	0.90	0.85–0.95[a]
Prenatal intercurrence[a]	2.60	1.11–6.40[a]	1.78	0.82–3.87
Childbearing interval (>24 months)	0.98	0.58–1.67	1.04	0.65–1.66
No prenatal visit	8.60	0.2–382.2	1.92	0.10–358.0
Number of prenatal visits (>6)	0.42	0.10–1.68	0.35	0.18–1.55
Surgical delivery (Caesarean)	1.68	0.76–3.68	1.57	0.79–3.11
No smokers in the house	0.72	0.36–1.43	0.67	0.39–1.15
No smokers in the child's bedroom	0.36	0.13–0.95[a]	0.63	0.39–1.15
Number of rooms at home (≥4)	0.97	0.75–1.26	0.95	0.70–1.11
Order of birth (≥2nd)	2.90	1.25–6.70[a]	3.03	1.66–5.53[a]
Family income (2 minimum wages)	1.26	0.55–2.90	1.23	0.60–2.54
Female gender	0.61	0.29–1.29	0.64	0.33–1.23
No previous use of antibiotics	0.63	0.28–1.41	0.52	0.25–1.07

[a]Significant associations

absence of smokers in the child's bedroom were significant clinical factors preventing the development of pneumonia. The mother's level of education <8 years and prenatal intercurrence were the variables found to be associated with the development of pneumonia and hospitalisation (potential risk factors).

Discussion

With regard to socio-demographic characteristics found in the present study, it was observed that children were predominantly male in the case group (53.9 %), a finding also reported in the literature regarding lung diseases [11, 12, 17]. The difference in mean age is corroborated by the available literature on pneumonia showing a higher incidence as well as higher mortality and morbidity rates in the first year of life [25]. Age over 5 years was shown to be a protective factor against pneumonia, which may be explained by the defence mechanisms these children develop over time (e.g. antibodies through vaccination), including their own immune response.

The parent's educational level, especially the mother's, has been demonstrated as being directly related to the risk of pneumonia [2, 20]. Another study showed that mothers living in areas with a high risk of pneumonia presented a low educational level [27]. Our findings also corroborate this trend, as the children of mothers who had studied less than 8 years were more likely (2.5 times) to have pneumonia. This finding can be explained by the fact that mothers are stronger decision makers regarding the health of their children [12].

The present study also found an association with the parent's smoking habits and people who smoke in the child's house or bedroom and the incidence of pneumonia. The number of smokers in the bedroom and the mother's smoking habits were associated with pneumonia and hospitalisation, showing that non-smoking mothers and the absence of smokers in the child's bedroom were factors protecting against the

Table 4 Associations between independent variables and response variable (pneumonia) through multivariate logistic regression analysis, considering children from 6 months to 5 years old

Variables	OR	95 % CI
Breastfeeding (>3 months)[a]	0.14	0.06–0.32[a]
Absence of comorbidities	0.28	0.06–1.31
Complications	0.09	0.01–1.09
Colour (ethnics)—White	0.80	0.41–1.88
Father's educational level (<8 years)	1.01	0.40–2.55
Mother's educational level (<8 years)[a]	2.78	1.11–6.96[a]
Non-smoking mother[a]	0.21	0.07–0.58[a]
Non-smoking father	0.66	0.23–1.83
Single child	0.51	0.22–1.14
Maternal weight gain (>10 kg)	1.96	0.87–4.43
House with water supply	2.34	0.02–19.4
House with basic sanitation	0.05	0.001–5.10
People in the house (≥2)	1.10	0.78–1.53
People in the bedroom (≥1)	1.35	0.86–2.13
Mother's age (>19 years)	0.99	0.92–1.06
Prenatal intercurrence[a]	2.51	1.02–6.18[a]
Childbearing interval (>24 months)	0.95	0.55–1.66
No prenatal visit	8.60	0.2–382.2
Number of prenatal visits (>6)	0.41	0.09–1.77
Surgical delivery (Caesarean)	1.08	0.46–2.50
No smokers in the house	0.73	0.35–1.50
No smokers in the child's bedroom	0.33	0.12–0.92[a]
Number of rooms at home (≥4)	0.96	0.72–1.29
Order of birth (≥2nd)	2.12	0.87–5.16
Family income (2 minimum wages)	1.24	0.28–1.35
Female gender	0.49	0.22–1.09
No previous use of antibiotics	0.61	0.27–1.35

[a] Significant associations

disease. These results are in agreement with findings reported elsewhere [21, 22].

In the present research, the number of pregnancies and the order of birth were also found to be associated with the development of pneumonia, according to a study by Fonseca et al. [6] which showed that the children of mothers who had seven or more pregnancies were more likely to have pneumonia compared to the children of mothers who had fewer pregnancies. In our study, both univariate and multivariate analyses showed that the order of birth was an important independent variable, that is, being born second (or third, fourth or fifth) increased the chance of pneumonia by 2.9 times. However, Nascimento-Carvalho et al. [19] found that the order of birth had no association with pneumonia. Our results can be explained by the fact that having a larger number of children leads the mother to devote less attention to each of her children; another explanation of the "concept of exposure" should be that many children have more possibilities to spread microorganisms via airborne particles [4, 6]. This hypothesis was also raised in another study [17] on the childbearing interval in mothers of children with respiratory infections. In the present study, the childbearing interval was not found to be associated with pneumonia in the multivariate analysis, supporting the results obtained by Fonseca [6] and Nascimento et al. [18].

In the present study, a difference was found in the mean age of the mothers of hospitalised children with and without pneumonia though a comparative analysis. However, by comparing the distributions of median values, such a difference was not observed. This may be explained by the great variability in the sample, evidenced by an asymmetric distribution, although the results are in accordance with findings reported in other studies conducted in southern Brazil [4, 28] which showed no association between maternal age and risk of death due to respiratory infections. Despite the fact that no association between maternal age and pneumonia was found in the present study, its importance as a predictor variable is unquestionable, since the literature shows that children of mothers younger than 20 years old and older than 35 years old are more likely to have pneumonia since they are less experienced in identifying the disease and in handling severe cases [28, 29]. However, in a study by Prietsch et al. [22], maternal age greater than 30 years old was a protective factor.

In our study, children of mothers who had complications during pregnancy were more likely (2.6 times) having pneumonia if compared to those mothers without complications. Galvão et al. showed a higher prevalence of respiratory and gastrointestinal infections in children of mothers who had complications in pregnancy. This finding requires further studies to better explain the possible association.

In the present study, breastfeeding lasting more than 3 months was found to be a protective factor against pneumonia. The role of breast milk in the protection against infectious diseases, including pneumonia, is well-described in the literature [15]. In a study conducted in Chile [16], the authors concluded that breastfeeding lasting less than 3 months is associated with a higher risk of pneumonia in infants younger than 6 months old, whereas research by Lopes and Berezin [15] showed that the lack of breastfeeding in the first 3 to 6 months of life was a risk factor for pneumonia. On the other hand, exclusive breastfeeding up to 6 months of age was the most contributing factor in the such protection, decreasing the chance of acquiring pneumonia by sevenfold. In a study performed in the USA [11], an increased risk of acute respiratory infection was found in children who had not exclusively breastfed for at least 4 months. In a study conducted in Brazil [6], breast milk was one of the factors protecting against death from respiratory infection. Another study, also performed in southern Brazil [3], showed that non-breastfed children had 17 times

more hospitalisations for pneumonia than those who had been exclusively breastfed in the first year of life.

Lack of comorbidity in the present study was a protective factor. The presence of previous respiratory infection is reported as a risk factor for severe pneumonia [25] and new episodes of pneumonia [6, 8]. Such relapses may involve several factors, such as deficiencies in the immune system, inborn defects or sequelae of previous disease [24].

Finally considering the present study, it is important to emphasise that the case–control approach is subject to biases, mainly in the selection phase. This might be the case in the present research regarding the hospitalisation of individuals with certain characteristics (e.g. low income), known as Berkson's paradox [14]. We sought to minimise such a bias with the selection of cases and controls from the same population, that is, children who were being treated in the same health care service over the same period of time. The mother's or caregiver's memory is another bias which might be overcome by asking questions on the child's recent health conditions and family, thus avoiding interfering with the results. However, one can identify other confusing variables such as family income, since most of the selected population had a family income lower than the minimum wage, including a low educational level among the mothers (the main caregivers). Therefore, these aspects should be taken into account as they influence the respondent's answers. In our research, the hospital from where the children had been selected was not evaluated, despite being a condition known to predispose to respiratory infections, such as pneumonia [28, 30], which might have a measurement bias. Similarly, one can consider that not only a potential selection bias might have occurred in the selection of hospitalised patients but also a measurement bias. This can be explained by the fact that patients with CAP are treated in hospitals only because of social reasons (i.e. low socioeconomic situation), young age or severe clinical condition [4, 23], thus overestimating these associations.

Overall, the results obtained in the present study are in accordance with findings reported elsewhere. The results of this work contribute favourably to the primary prevention and promotion of health aimed at acting more efficiently on the risk factors related to the health–disease process, not only in cases of CAP but also in the majority of infectious diseases in children.

Conflict of interest The authors declare no conflict of interest

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