Original Article

Hierarchical approach to determining risk factors for pneumonia in children*

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Background: Acute respiratory infection, especially pneumonia, plays an important role in childhood morbidity and mortality, as much in Brazil as in the world.

Objective: To identify, using a hierarchical logistic regression model, the risk factors for hospitalization in children with pneumonia.

Method: A hospital-based case-control study was performed at the University Hospital in Taubaté, SP between May and December of 2001. The cases studied were children diagnosed and hospitalized with pneumonia, and the controls were children hospitalized for causes other than respiratory infection. A hierarchical logistic regression model was applied. The model groups variables into 4 levels: socioeconomic; reproductive and gestational; environmental; and nutritional. After the univariate analysis, variables with *p* values < 0.20 were introduced into each level of the model, and those variables that maintained *p* values < 0.10 remained in the final model. Data compilation and analysis were performed using SPSS v.10 software.

Results: The final hierarchical logistic regression model identified the variables: level of education of the father, age of the mother, number of persons living in the house, birth weight, weight relative to age, and Z score as risk factors for hospitalization with pneumonia.

Conclusions: Interventions for the variables evaluated in this study can decrease the odds for hospitalization due to pneumonia.

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INTRODUCTION

Acute respiratory infection, especially pneumonia, is responsible for a significant portion of deaths among children in developing countries. It has been estimated that approximately 5 million children younger than 5 years of age have died, and death from pneumonia accounted for 70% of these deaths[1].

In 2000, Brazilian Health Ministry data showed that 1530 (10.2%) of the 15,000 deaths among children younger than 10 years of age were caused by respiratory disease[2].

Respiratory diseases also increase expenditures by the *Sistema Único de Saúde* (Unified Health System). In 2000, the cost of hospitalization caused by respiratory disease was approximately R$45 million (approximately US$18 million) in the state of São Paulo alone[3].

Notable among the risk factors for hospitalization are malnutrition[4], lack of breastfeeding[5], low educational level of the parents, low birth weight, young age of the mother, low weight gain during gestation, smokers in the home, parity, and an overcrowded household[6-8].

Therefore, since there are many risk factors, the decision to include risk variables should not be based on statistical significance also but should also be determined through a hierarchical conceptual framework that includes various levels and maintains an interrelation[9].

In a hierarchical approach, distal determiners show their direct action on the dependent variable and also show their effects on factors that compose the subsequent levels. On the other hand, factors at a lower level are controlled by those at the higher levels and, in turn, control factors at even lower levels. However, they also act directly on the dependent variable[10].

Since there are no known studies on risk factors for pneumonia or for hospitalization due to pneumonia in the state of São Paulo, the objective of the present study was to identify, using a hierarchical approach, these risk factors for hospitalization due to pneumonia in a university teaching hospital.

METHODS

A hospital-based case-control epidemiological study was performed. The cases studied were children hospitalized with pneumonia on the pediatric ward of the *Hospital Universitário de Taubaté* (Taubaté University Hospital), in the state of São Paulo.

The controls were recruited from among children hospitalized on the same ward during the same period for causes other than respiratory infection, as well as from among children undergoing routine early-childhood examinations in the Pediatric Department or being treated in any other department (except Pulmonology).

The study period was from May to December of 2001.

Inclusion criteria were defined as hospitalized children diagnosed with pneumonia based on clinical evidence – cough, fever, chest pain, rales upon auscultation – and chest X-rays that confirmed this clinical suspicion. A specialist in pediatric radiology performed the chest X-rays.

The size of the sample was calculated using a ratio of 1.5 controls to 1 case, based on an alpha error of 5% and a beta error of 20%, sufficient for detecting an odds ratio (OR) equal to 1.7 and estimating an exposure of 25% among the controls. The original sample comprised 95 cases and 143 controls. We chose to enlarge this sample by 10%. We used the Epitable tool of the Epi-Info 6.04 software to make this calculation.

Mothers were informed about the objective of the study, which did not involve any risk to the children and, after giving consent, answered a structured questionnaire. The Ethics Committee of the university hospital approved the study.

Independent variables were categorized into levels.

The first level (level 1) was composed of the sociodemographic variables: family income (either 0 to 2 minimum salaries, 2.1 to 4 minimum salaries or more than 4 minimum salaries) and educational level of the father and the mother (either 0 to 4 years of schooling, 5 to 8 years of schooling or more than 8 years of schooling).

The second level (level 2) was composed of the maternal and gestational reproductive variables: age of the mother (either less than 20, 20 to 34 or over 34); interval between the previous and current pregnancy (either less than 24 months or more than 24 months); weight gain during gestation (either less than 10 kg or more than 10 kg); and birth order (whether the first child, second child, third child, etc.)

TABLE 1.
Distribution of study cases and controls according to socioeconomic variables, and the respective odds ratios, 95% confidence intervals and *p* values

Level 1	Study cases	Controls	OR	95% CI	*p*
Family income ($p = 0.39$)#					
≤2 SM	39	57	1.00		
2.1 to 4 SM	35	55	0.93	0.50-1.75	0.92
> 4 SM	10	22	0.66	0.26-1.68	0.39
Level of education of the mother ($p = 0.03$)#					
≤ 4 years of schooling	31	33	2.16	1.02-4.60	0.04
5-8 years of schooling	51	65	1.81	0.94-3.49	0.08
> 8 years of schooling	23	53	1.00		
Level of education of the father ($p = 0.01$)#					
≤ 4 years of schooling	28	37	2.81	1.22-6.52	0.012
5-8 years of schooling	49	59	3.08	1.45-6.62	0.002
> 8 years of schooling	14	52	1.00		

#chi-square test for linear tendency
OR: odds ratio; 95% CI: 95% confidence interval; SM: minimum salary

TABLE 2
Distribution of study cases and controls according to maternal and gestational reproductive variables, and the respective odds ratios, 95% confidence intervals and *p* values

Level 2	Cases	Controls	OR	95% CI	*p*
Age of the mother ($p = 0.002$)#					
≤ 19	16	11	2.00	0.82-4.94	0.14
20-34	74	102	1.00		
> 34	17	41	0.47	0.23-0.97	0.04
Interval between pregnancies§					
≤ 24 months	20	27	1.18	0.56-2.52	0.76
> 24 months	50	57			
Weight gain during gestation					
≤ 10 kg	63	54			
> 10 kg	81	35	0.50	0.28-0.90	0.02
Birth order ($p = 0.002$)#					
First child	33	70	1.00		
Second child	34	53	1.36	0.72-2.58	0.39
Third child or later	37	31	2.53	1.28-5.01	0.006

#chi-square test for linear tendency §Primiparous women excluded
OR: odds ratio; 95% CI: 95% confidence interval

The third level (level 3) was composed of the environmental variables: number of people in the household; number of people in the bedroom where the child sleeps; number of smokers in the household; and number of people in the bedroom where the child sleeps. The final level (level 4) was composed of nutritional variables.

The distal nutritional variable was birth weight, considered low if less than 2500 g and normal if greater than that.

The proximal nutritional variables were breastfeeding and Z score for weight-age (at time of hospitalization if the child was hospitalized or at the time of the interview if the child was an outpatient at the clinic). This variable was categorized into scores below zero and scores equal to or greater than zero.

Initially, a univariate analysis was performed among independent variables according to the case or control situation. Odds ratios were estimated, 95% confidence intervals were calculated, and *p* values were determined.

Subsequently, level-1 variables presenting values of $p < 0.20$ in the univariate analysis were introduced only once. Variables presenting values of $p < 0.10$ at this moment in the hierarchical analysis remained at level 1.

Maintaining the level-1 variables, we studied level-2 variables presenting values of $p < 0.20$ in the univariate analysis. These variables were simultaneously introduced into the model, independently of changes in the statistical significance of the values of the level-1 variables already in the model. Level-2 variables presenting values of $p < 0.10$ remained in the model. These level-2 variables were thereby adjusted for the level-1 variables that remained at level 1.

Maintaining the level-1 and level-2 variables, we introduced, as before, level-3 variables presenting p values < 0.20, and, regardless of possible changes in the statistical significance of level-1 and level-2 variables, level-3 variables presenting p values < 0.10 remained in the model.

Finally, the nutritional variables of level 4 were introduced in the same manner as the previous ones, and those that maintained a p value < 0.10 remained in the model.

The hierarchical analysis was thereby completed.

We used the chi-square test for the study of ordinal, categorical variables such as family income, educational level of the father and the mother, age of the mother and birth order.

We used the SPSS v.10 software program for the logistic regression analysis.

RESULTS

The study comprised 103 children diagnosed with pneumonia in the study group and 156 children in the control group.

There were 139 males (86 in the control group and 53 in the case group) and 120 females (70 in the control group and 50 in the case group). This distribution presented no differences (p = 0.65).

Values of the sociodemographic variables found in the univariate analysis are shown in Table 1. We observed the significance of lower educational

TABLE 3
Distribution of study cases and controls according to environmental variables, and the respective odds ratios, 95% confidence intervals and p values

Level 3	Cases	Controls	OR	95% CI	p
Number of people in the room where the child sleeps					
1 person	46	78	1.30	0.76-2.22	0.37
2 or more people	59	77			
Number of people in the household					
4 people	42	92	2.22	1.29-3.83	0.003
5 or more people	63	62			
Smokers in the household					
Yes	42	40	1.88	1.06-3.34	0.03
No	63	113			
Smokers in the room where the child sleeps					
Yes	42	39	1.93	1.09-3.43	0.02
No	63	113			

OR: odds ratio; 95% CI: 95% confidence interval

TABLE 4
Distribution of study cases and controls according to distal and proximal nutritional variables, and the respective odds ratios, 95% confidence intervals and p values

Level 4	Cases	Controls	OR	95% CI	p
Low birth weight	21	14	2.63	1.21-5.88	0.012
Normal birth weight	78	138			
Breastfeeding					
Yes	88	136	0.76	0.36-1.63	0.56
No	17	20			
Z-score weight/age < 0	71	80	2.17	1.23-3.85	0.005
Z-score weight/age ≥ 0	30	74			

OR: odds ratio; 95% CI: 95% confidence interval

TABLE 5
Final hierarchical analysis model to determine risk factors for hospitalization in children with pneumonia, and the respective odds ratios, 95% confidence intervals and *p* values

	OR	95% CI	*p*
Educational level of the father			
≤ 4 years of schooling	2.81	1.22 – 6.02	0.01
5-8 years of schooling	3.08	1.45 – 6.62	
> 8 years of schooling	1.00		
Age of the mother [a]			
≤ 19	2.00	0.82 – 4.94	0.02
20-34	1.00		
> 34	0.47	0.23 – 0.97	
People in the household			
≤ 4 [b]	0.45	0.26 - 0.79	0.005
Low birth weight [c]	2.03	0.92 - 4.54	0.08
Z-score weight/age ≥ 0 [d]	1.98	1.05 - 3.72	0.03

Empty model deviation = 121.25; Saturated model deviation = 95.92; c^2 = 25.3 ($p < 0.001$)
[a]Model 1 = Educational level of the father + Age of the mother
[b]Model 2 = Model 1 + Number of people in the household
[c]Model 3 = Model 2 + Low birth weight
[d]Model 4 = Model 3 + Z-score weight/age ≥ 0
OR: odds ratio; 95% CI: 95% confidence interval

level (0 to 4 years of schooling) of the mother and father. The odds for such parents to have a child hospitalized with pneumonia were 2 to 3 times higher.

Table 2 shows maternal and gestational reproductive variables. Likewise, age of the mother and birth order are notable for their statistical significance. Younger mothers are twice as likely to have a child hospitalized due to pneumonia when compared to mothers who are from 20 to 34 years of age. The higher the rank in birth order, the greater the chance for hospitalization due to pneumonia.

Environmental variables (level 3) are shown in Table 3. A high number of people in the household, a high number of smokers in the household or a high number of smokers in the room where the child sleeps nearly double the odds for hospitalization.

Nutritional variables showed the importance of low birth weight, a risk factor that nearly triples the odds for hospitalization, as well as that of the weight/age nutritional score, which, when low, increases the odds for hospitalization. Breastfeeding was a protective factor against hospitalization, although not statistically significant (Table 4).

Table 5 shows the final analysis model. We can see that the educational level of the father directly acts as a risk factor for hospitalization due to pneumonia and affects the other variables for the risk of hospitalization due to pneumonia. The table also shows the importance of nutritional factors, such as birth weight and Z score, which are mediated by factors on the levels above. Low birth weight directly acts on the risk but indirectly acts through its influence on the nutritional state. This last variable is controlled by the others.

DISCUSSION

This is the first hospital-based study of risk factors for pneumonia involving children treated at a university teaching hospital that provides care exclusively for *Sistema Único de Saúde* users in the state of São Paulo.

Selection bias, as well as recall bias, is especially likely in case-control studies. In the present study, selection bias should have been minimized since both study cases and controls were recruited from the university hospital that provides care for patients using the *Sistema Único de Saúde*. Recall bias was certainly avoided since questions dealt with the information about the children (which the mothers knew well), as well as with maternal, gestational and environmental reproductive data.

Since there have been no previous studies of risk factors for hospitalization of children due to pneumonia in the state of São Paulo, these findings may provide information for possible interventions in order to reduce the number of hospitalizations due to pneumonia in children. It is notable that, in 2000, the number of hospitalizations due to

respiratory diseases was approximately 130,000, and that this number represents approximately 32% of the total number of hospitalizations reported by the *Sistema Único de Saúde*[3].

The hierarchical analysis showed that, of the socioeconomic and demographic variables, the educational level of the father was more important than the educational level of the mother. Victora et al. reported similar results[6]. The chance of hospitalization due to pneumonia is three times higher if the father has less than 9 years of schooling. We were unable to find a satisfactory explanation for this in the literature.

In the multivariate model, the educational level of the mother was adjusted for the other variables of the level, thereby losing its statistical significance. The educational level of the parents proved important when compared, in terms of severity and length of hospital stay, to two groups of children hospitalized with pneumonia in two hospitals in Salvador, Bahia[11].

Family income presented no statistical significance either in the univariate or in the multivariate analysis. It is possible that, if data were categorized in a different way, causality might be seen between income and chance of hospitalization with pneumonia. However, it is equally possible that the data provided by the mothers do not reflect the reality.

Young age of the mother doubled the chance for hospitalization due to pneumonia when compared to mothers from 20 to 34, and quadrupled the chance compared to those older than 34. Possible explanations for this are lack of experience in childcare and difficulty in identifying more severe conditions. However, there is no consensus on this matter[6,16,17].

Unlike studies carried out in the south of Brazil[6,17], interval between pregnancies presented no statistical significance, and birth order, which was significant in the univariate analysis, lost its significance after being adjusted for the variables of the same level and of the level above.

The hierarchical analysis also showed the role of the number of people inhabiting the same household. This situation has been considered a risk factor for pneumonia[9]. This variable may act as a risk factor due to a higher possibility of pathogen transmission through respiratory droplets[12].

After adjustment, no associations were found between the presence of smokers in the household or in the room where the child sleeps. This is in contrast to the findings of other studies[9,13-15] that might not have taken into consideration some possible confounding factors but is in agreement with the study conducted by Victora et al.[6] It is possible that the passive smoking effect is more closely related to other respiratory diseases such as bronchitis and bronchiolitis, neither of which were analyzed in the present study.

Low birth weight was identified as a risk factor for hospitalization due to pneumonia and remained significant after being adjusted for other variables. This finding corroborates those form other studies[4,6,17]. The odds for hospitalization due to pneumonia are doubled for low birth weight children. The explanation for this is that there is a decreased immune response, impaired pulmonary function due to smaller diameters of the upper airways and a higher tendency for peripheral airway obstruction.

In contrast to the findings of other studies performed in Brazil[4-6,17], breastfeeding presented no statistical significance at this level.

Finally, Z score for weight/age was also an important risk factor. Children with a score lower than 0 were twice as likely to be hospitalized when compared to children with a score equal to or greater than 0, even after being adjusted for all the other variables. These findings are similar to those of other studies in the literature[4,6]. A possible explanation is that undernourished children have impaired immune responses and are more likely to have more severe infections than are well-nourished children[18]. Even if some weight loss occurs due to pneumonia, it would not be noticed as quickly as in, for example, cases of diarrhea.

Therefore, measures taken in order to prevent low weight and to preserve the nutritional state, interventions implemented during routine pre-natal and early-childhood examinations, may reduce the odds for hospitalization due to pneumonia within a short period of time. These measures, although well known, have not been implemented in the realm of public health.

Interventions intended to increase the educational level and age of the mother at the time of delivery through prevention of pregnancy during adolescence are measures that must be

evaluated for long periods in order to properly judge the results.

Improved housing conditions, a situation probably influenced by income, in which a smaller number of people inhabit the same household, would, for example, have an impact on reducing birth rates. This calls for greater investments in education and in social programs.

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