Factors Associated with Respiratory Illness in Children and Young Adults with Cerebral Palsy

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Objective To describe associations between respiratory illness and its potential predictors in children and young adults with cerebral palsy (CP).

Study design Cross-sectional survey of self- and caregiver-reported respiratory symptoms for individuals aged up to 26 years with CP. Respiratory illness was indicated by 2 outcomes: (1) ≥1 respiratory hospitalizations in the past year; and (2) ≥2 courses of antibiotics for respiratory symptoms in the past year. ORs were calculated using univariate and multivariate logistic regression.

Results There were 551 participants, aged 1-26 years, distributed across all gross motor function classification scale (GMFCS) levels. In univariate analyses, factors significantly associated with respiratory hospitalizations were weekly respiratory symptoms (OR 2.31, 95% CI 1.78-3.00), respiratory symptoms during meals (OR 3.23, 95% CI 1.50-5.80), gastroesophageal reflux (OR 3.01, 95% CI 1.71-5.31), coughing or choking on saliva (OR 4.36, 95% CI 2.38-8.01), current asthma (OR 3.56, 95% CI 1.97-6.42), age (0-3 years) (OR 3.24, 95% CI 1.19-8.80, compared with 13-17 years), seizures (OR 3.45, 95% CI 1.96-6.08), and scoliosis (OR 2.14, 95% CI 1.16-3.97). Nonambulatory individuals (GMFCS IV-V) were at significantly increased risk of hospitalizations only if they had food modifications and/or nasogastric or gastrostomy tube feeds (OR 5.36, 95% CI 2.89-9.96, compared with GMFCS I-III with no food modifications and no tube). All factors, except seizures and scoliosis, were significantly associated with multiple courses of antibiotics in univariate analyses.

Conclusions Oromotor dysfunction is strongly associated with respiratory illness in patients with CP. *(J Pediatr 2016;168:151-7)*.

Cerebral palsy (CP) is defined by movement impairment of cerebral origin.[1] It is the most common childhood physical disability with an incidence in developed countries of 2-2.5 per 1000 live births.[2-4] Although CP manifests itself during childhood, it is a lifelong condition with heterogeneous presentation in levels of impairment and disability. Comorbidities are common and include epilepsy, scoliosis, dysphagia, and impairments of sensation, cognition, communication, and behavior.[1] Despite numerous improvements in medical, surgical, and therapeutic interventions, survival in CP has not improved in the past 40 years.[5,6]

Respiratory disease, in particular pneumonia, is the leading cause of death[7,8] and hospitalization[9,10] in children and young adults with CP. The reasons for this population's vulnerability to respiratory disease are complex and not understood fully. Various potential risk factors have been suggested, including dysphagia leading to aspiration of saliva and/or nutritional intake, impaired motor function, absence of or a reduction in protective reflexes related to swallowing, and impairment in muscle strength and coordination pertaining in particular to the respiratory muscles. In addition, common comorbidities in individuals with CP also may increase risk of respiratory illness. For example, gastroesophageal reflux may lead to aspiration pneumonia or to chronic respiratory symptoms, which can mimic asthma, and scoliosis causes reduced lung capacity and may make individuals more susceptible to respiratory illness.[11] Some of these risk factors are manageable. However, there are no published data to indicate which combination of factors best predicts respiratory morbidity in children and young adults with CP. This information is needed to guide interventions to reduce their respiratory morbidity and mortality. The present study aims to describe the relationships between severe respiratory illness and its potential predictors in children and young people with CP.

CP	Cerebral palsy
GMFCS	Gross motor function classification scale
MoI	Method of nutritional intake

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Methods

This was a cross-sectional survey. All individuals living in Western Australia between 0 and 26 years of age inclusive and meeting the criteria for CP were eligible to participate. Potential participants, who had been identified from the databases of the state pediatric hospital and the major CP community service provider, were invited by mail with follow-up phone calls and by personal contact to participate in the study. Information about the study was also distributed widely using mail-outs, newsletters, group e-mails, and posters through tertiary institutions, disability service providers, supported employment agencies, alternatives to employment services, accommodation and respite services, and sports and recreation clubs. Recruitment occurred between November 2011 and June 2012. The survey was completed on paper, online, or by phone or face-to-face interview either by competent participants over 18 years of age or by a parent or caregiver. Ethics approval for this study was obtained from the Princess Margaret Hospital for Children Ethics Committee and the Department of Health Western Australian Human Research Ethics Committee.

All measures were self-reported or parent/caregiver-reported. Two separate outcome measures were chosen to indicate severe respiratory morbidity: (1) ≥1 hospital admissions for respiratory symptoms in the previous 12 months; and (2) ≥2 courses of antibiotics for respiratory symptoms in the previous 12 months. Potential predictor variables included the following: frequency of coughing, frequency of sounding chesty or phlegmy, frequency of sounding wheezy, frequency of snoring, method of nutritional intake (MoI), presence of respiratory symptoms during meals, presence or history of gastroesophageal reflux, presence of seizures, body weight estimation, coughing or choking on saliva, diagnosis of scoliosis, current asthma, presence of smoker in the household, age, sex, and gross motor function classification scale (GMFCS) classification.[12] To assess GMFCS the GMFCS Family Report Questionnaires were used <12 years of age, and the GMFCS Expanded and Revised Descriptors and Illustrations for Children between their 12th and 18th Birthdays were used for all those >12 years. The **Appendix** (available at www.jpeds.com) shows the response options and coding for all variables.

As no published data collection instrument existed to determine the prevalence of respiratory symptoms in this population, our choice of variables was based on research literature concerning respiratory morbidity in CP and other clinical populations and the clinical expertise of the multidisciplinary research team and their colleagues. The questionnaire was initially pilot-tested face to face with 25 individuals who had CP, their parents, caregivers, and nursing staff, who were asked to comment critically on their experience. On the basis of their input, the questionnaire was revised and piloted further with three additional individuals with CP.

Statistical Analyses

The population was described in terms of mean ± SD, and frequencies and percentages of all collected variables. In addition, GMFCS was dichotomized into ambulators (levels I-III) and nonambulators (levels IV-V). MoI was also dichotomized into those who had food modifications (such as thickened or puréed foods and thickened drinks) and/or nasogastric or gastrostomy tube feeds and those who did not have any food modifications or tube. These 2 dichotomous variables were then combined into a variable consisting of 4 categories: (1) GMFCS I-III and no food modifications or tube; (2) GMFCS I-III and food modifications and/or tube; (3) GMFCS IV-V and no food modifications or tube; and (4) GMFCS IV-V and food modifications and/or tube. This combination variable (GMFCS/MoI) was created in order to circumvent the problems of collinearity and sparse data. χ^2 analysis was used to assess statistical significance of associations between descriptive variables, predictors, and outcomes. When low cell numbers were present ($n < 5$), Fisher exact χ^2 test was used.

ORs (with 95% CIs) were calculated using univariate logistic regression to further explore the relationship between the identified risk factors and each of the outcomes (respiratory hospitalizations and antibiotic use). Multivariate logistic regression followed to create a final model. A stepwise approach using backwards elimination was used, as outlined by Hosmer and Lemeshow.[13] Variables were included in the initial model if the univariate test resulted in a P value of <.25 or the variable was considered clinically important. For variables with several categories (such as age group), the likelihood ratio statistic was used to assess the overall contribution of the variable to the final model. Variables that did not contribute to the fit of the model were dropped from the model. Contribution to the model was assessed through examination of the Wald statistic for each variable, comparing each estimated coefficient from the multivariate model with the univariate model, and reviewing the impact of the removal of the variable on the other estimated coefficients. If a variable was eliminated, the new model then was compared with the older (larger) model using the likelihood ratio test. Once a preliminary main effects model had been identified, any variable that had not been selected was added back into the model. This step assisted in identifying variables that were not significantly related to the outcome in isolation but did make an important contribution in the presence of other variables. For the continuous variable of "respiratory symptoms on a weekly basis," the assumption of linearity in the logit was confirmed. Interaction between variables in the final model was considered and assessed with the likelihood ratio statistic. Statistical significance level was set at $P < .05$. All statistical analysis was performed using Stata v 10.1 (StataCorp, College Station, Texas).

Results

Usable questionnaires were received from 551 eligible participants aged 1-26 (11.1 ± 5.9) years. Given the recruitment