



Growth, lung function, and physical activity in schoolchildren who were very-low-birth-weight preterm infants

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INTRODUCTION

Surfactant therapy and prenatal steroid use have been reported to result in a significant reduction in mortality among very-low-birth-weight (VLBW) infants.⁽¹⁾ However, many preterm infants require prolonged oxygen supplementation or mechanical ventilation, which can lead to irreversible damage to the lung parenchyma.⁽²⁾

Controversy remains regarding the effects of prematurity, low birth weight, and certain neonatal factors on lung function in school-age children, despite the fact that several studies have examined this issue. Although some studies have shown a reduction in FEV₁, FVC, and lung volumes in preterm infants,^(3,4) others have shown preserved lung function during childhood.^(5,6) To date, there have been no studies conducted in Brazil and evaluating lung function in school-age children who were VLBW infants.

In preterm infants, the natural development of the lungs and airways is affected by the fact that part of the process of lung development occurs after birth.⁽⁷⁾ In an immature respiratory system, remodeling patterns occur in accordance with the affected developmental stage.⁽⁸⁾ Previous studies have shown that neonatal and perinatal factors can trigger a sequence of events that

ABSTRACT

Objective: To compare somatic growth, lung function, and level of physical activity in schoolchildren who had been very-low-birth-weight preterm infants (VLBWPIs) or normal-birth-weight full-term infants. **Methods:** We recruited two groups of schoolchildren between 8 and 11 years of age residing in the study catchment area: those who had been VLBWPIs (birth weight < 1,500 g); and those who had been normal-birth-weight full-term infants (controls, birth weight ≥ 2,500 g). Anthropometric and spirometric data were collected from the schoolchildren, who also completed a questionnaire regarding their physical activity. In addition, data regarding the perinatal and neonatal period were collected from the medical records of the VLBWPIs. **Results:** Of the 93 schoolchildren screened, 48 and 45 were in the VLBWPI and control groups, respectively. No significant differences were found between the groups regarding anthropometric characteristics, nutritional status, or pulmonary function. No associations were found between perinatal/neonatal variables and lung function parameters in the VLBWPI group. Although the difference was not significant, the level of physical activity was slightly higher in the VLBWPI group than in the control group. **Conclusions:** Among the schoolchildren evaluated here, neither growth nor lung function appear to have been affected by prematurity birth weight, or level of physical activity.

Keywords: Premature birth; Birth weight; Respiratory function tests; Motor activity; Pediatrics.

can affect lung structures and increase the incidence of respiratory disease.^(7,9)

Among school-age children, the risk of health complications and delayed development is higher in those who were preterm infants and in those born at extremely low birth weight than in those who were full-term infants.⁽¹⁰⁾ In addition, studies suggest that, in preterm infants, catch-up growth is delayed and the risk of growth restriction in the first years of life is high,^(11,12) and that the subnormal weight and height observed in the first months of life can persist throughout childhood, adolescence, and adulthood.⁽¹³⁾

In the last two decades, there has been a significant reduction in the level of physical activity and an increase in sedentary behavior among pediatric patients.^(14,15) This can be attributed to changes in the types of activities in which young people engage, active activities involving increased energy expenditure having been replaced with long hours spent using the computer, playing video games, and watching television.⁽¹⁴⁾ However, there is currently little information regarding the level of physical activity among schoolchildren who were preterm infants, low-birth-weight infants, or both.^(16,17)

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The present study was motivated by the contradictory findings regarding lung function in school-age children who were low-birth-weight preterm infants, the possibility of retardation of growth (weight and height) in such children, and the significant changes in the types of activities in which they engage. The specific objectives of the study were to evaluate growth, lung function, and the level of physical activity in schoolchildren who were in the 8- to 11-year age bracket and who had been VLBW preterm infants and to compare their growth, lung function, and level of physical activity with those of schoolchildren who were in the same age bracket and who had been normal-birth-weight (NBW) full-term infants.

METHODS

This was a case-control study. The study included schoolchildren who were in the 8- to 11-year age bracket at the time of the study, who had been preterm infants whose birth weight was $\leq 1,500$ g, and who had been admitted to the Caxias do Sul General Hospital Neonatal ICU, in the city of Caxias do Sul, Brazil, between January of 2001 and December of 2005. For logistical reasons, only children residing in municipalities located within up to 100 km of Caxias do Sul were invited to participate in the study. Prospective participants were contacted by telephone.

The control group comprised children who had been full-term infants (≥ 37 weeks of gestational age) whose birth weight was $\geq 2,500$ g, who had no respiratory symptoms, as determined by the International Study of Asthma and Allergies in Children questionnaire,⁽¹⁸⁾ and who were recruited from among those attending public schools in Caxias do Sul. Children with heart disease, those with neuromuscular disease, those with cognitive limitations, and those who were unable to perform spirometry were excluded from the study.

Data were collected by two trained researchers at the University of Caxias do Sul in the period between July and December of 2013. The study was approved by the Research Ethics Committee of the Pontifical Catholic University of Rio Grande do Sul (Protocol no. 12323413.7.0000.5336), located in the city of Porto Alegre, Brazil, and the parents or legal guardians of the children who agreed to participate in the study gave written informed consent.

Data regarding the perinatal and neonatal periods for the children who had been VLBW preterm infants (the VLBWPI group) were collected from the neonatal ICU database. We collected data on the following variables: use of antenatal corticosteroids; premature rupture of membranes; duration of oxygen therapy; length of hospital stay; birth weight; use of continuous positive airway pressure; hyaline membrane disease; and surfactant use.

Weight was measured with a digital scale (Glass 1 FW; G-Tech, Rio de Janeiro, Brazil), and height was measured with a portable stadiometer (Alturaexata; TBW, São Paulo, Brazil). On the basis of height and

weight, nutritional status was normalized to height-for-age, weight-for-age, and BMI-for-age Z scores.⁽¹⁹⁾

Spirometry was performed with a portable spirometer (Koko; Ferraris Respiratory, Louisville, CO, USA). All tests were performed in accordance with the American Thoracic Society standards and acceptability and reproducibility criteria.⁽²⁰⁾ The children were verbally encouraged to perform a maximal expiratory maneuver at maximal effort following a maximal inspiratory maneuver.⁽²⁰⁾ The following spirometric parameters were assessed: FVC; FEV₁; and FEF_{25-75%}.^{*} The results were expressed as absolute values and normalized to Z scores.⁽²¹⁾

The level of physical activity was assessed by an adapted questionnaire consisting of items regarding the activities performed in the last seven days.⁽¹⁴⁾ The questionnaire gathered information on the type of activity, time spent commuting to school, work, or both, and frequency of/time spent in leisure-time physical activity. On the basis of their level of physical activity, the schoolchildren were classified as active (> 300 min/week) or inactive (≤ 300 min/week); those who were classified as having sedentary behaviors were subdivided into two groups, on the basis of their daily screen time (> 2 h/day or ≤ 2 h/day).⁽²²⁾

A sample of 25 individuals per group was calculated to be sufficient to detect a 14% difference in percent predicted FEV₁, a standard deviation of 12% for the control group and of 17% for the VLBWPI group being assumed (on the basis of a previous study, with a power of 90% and a significance level of 5%).⁽²³⁾ Given the possibility of losses, the number of individuals per group was increased to 30, totaling 60 participants.

The study variables were assessed by the Kolmogorov-Smirnov test. Variables with normal distribution were expressed as mean and standard deviation, whereas those with non-normal distribution were expressed as median and interquartile range. Categorical variables were expressed as absolute and relative frequencies. The study outcomes were compared between the two groups by the Student's t-test for independent samples, the Wilcoxon U test, and Pearson's chi-square test. Univariate and multivariate linear regression models were used in order to evaluate the association between outcome variables (FEV₁, FVC, and FEF_{25-75%}) and predictor variables (birth weight, length of hospital stay, gestational age, premature rupture of membranes, use of surfactant, use of antenatal corticosteroids, duration of oxygen therapy, duration of mechanical ventilation, use of continuous positive airway pressure, and hyaline membrane disease). All analyses were performed with the Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, USA), and differences were considered significant at $p < 0.05$.

RESULTS

Of the 338 VLBW preterm infants admitted to the neonatal ICU during the data collection period, 219 (64.79%) survived. Of those, 91 (41.55%) were

located, and only 62 (28.31%) were selected for the study. Figure 1 shows the data regarding the selection of participants in the VLBWPI group.

Of the 62 VLBW preterm infants selected, 7 were excluded because of technically inadequate spirometry tests and 7 were excluded because of cognitive deficits that prevented them from undergoing spirometry. Therefore, 48 (77.41%) participated in the study. Table 1 shows the information regarding the perinatal and neonatal periods for the VLBWPI group. There were no significant differences between the individuals who were included in the VLBWPI group and those who were not regarding neonatal and perinatal factors.

In addition to the individuals who were selected for inclusion in the VLBWPI group, 52 controls were selected. Of those, 5 were excluded because they failed spirometry and 2 were excluded because they had cognitive deficits, a total of 45 controls (86.53%) being included in the study. Therefore, the final study sample consisted of 93 children: 48 in the VLBWPI

group and 45 in the control group. There were no significant differences between the two groups regarding anthropometric characteristics or nutritional status (Table 2).

With regard to lung function data, there were no significant differences between the VLBWPI group and the control group regarding mean spirometric variables (Table 3). Most of the study sample had normal spirometric values, i.e., Z scores above -1.645 for the variables analyzed. In the VLBWPI group, 6 participants had reduced $FEV_{1.}$ Mean gestational age (28.1 ± 0.9 weeks; $p = 0.006$) and mean birth weight ($1,015.0 \pm 122.7$ g; $p = 0.008$) were significantly lower in those 6 than in the remaining 42 participants in the VLBWPI group. Although there were differences regarding the length of hospital stay [median number of days = 54.0 (42.0-66.0); $p = 0.249$] and the need for oxygen therapy for more than 28 days [$n = 3$ (60%); $p = 0.083$], they were not significant. The univariate and multivariate linear regression analyses revealed no significant associations of perinatal and neonatal factors with lung function data in the schoolchildren in the present study. Table 4 shows the associations found in the univariate analysis.

With regard to the level of physical activity, 34 (36.5%) of the participants were classified as active, and 59 (63.4%) were classified as inactive. Although the level of physical activity was slightly higher in the VLBWPI group than in the control group, the difference was not significant ($p = 0.055$; Figure 2A). In the VLBWPI and control groups, the most common leisure-time physical activities were soccer (37.5% vs. 22.2%; $p = 0.108$), running (27.9% vs. 22.2%; $p = 0.936$), and cycling (14.6% vs. 31.1%; $p = 0.057$). The mean time spent in active commuting was 20.55 ± 5.89 min and 19.75 ± 6.78 min ($p = 0.737$), respectively. Finally, although screen time was found to be > 2 h/day in 90 (96.7%) of the participants, there were no significant differences ($p = 0.596$) between the VLBWPI group and the control group regarding daily screen time (Figure 2B).

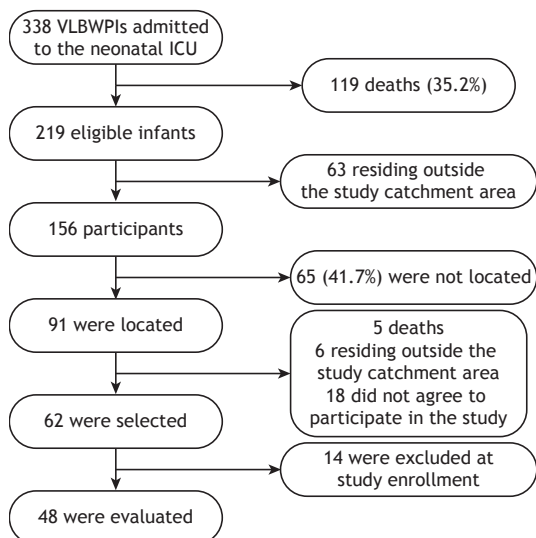


Figure 1. Flowchart of inclusion and exclusion of very-low-birth-weight preterm infants (VLBWPIs).

Table 1. Comparison of perinatal and neonatal variables between the very-low-birth-weight preterm infants who were included in the present study and those who were not.^a

Variable	Included in the study (n = 48)	Not included in the study (n = 171)	p
Antenatal corticosteroid use	31 (64.6)	100 (58.5)	0.379
Surfactant use	31 (64.6)	100 (58.5)	0.349
HMD	34 (70.8)	112 (65.5)	0.324
MV	31 (64.6)	100 (58.5)	0.349
PROM	06 (12.5)	25 (14.6)	0.720
Oxygen therapy > 28 days	09 (18.7)	38 (22.2)	0.623
CPAP	27 (56.2)	105 (61.4)	0.317
Length of hospital stay, days ^b	46.0 (35.5-60.0)	43.0 (36.0-57.0)	0.571
Birth weight, g ^c	1.210.42 ± 168.72	1.226.07 ± 210.85	0.278
Gestational age, weeks ^c	30.4 ± 4.5	32.0 ± 5.8	0.615

HMD: hyaline membrane disease; MV: mechanical ventilation; PROM: premature rupture of membranes; and CPAP: continuous positive airway pressure. ^aValues expressed as n (%), except where otherwise indicated. ^bValues expressed as median (interquartile range). ^cValues expressed as mean ± SD.

Table 2. Comparison of anthropometric characteristics and nutritional status between the schoolchildren who had been very-low-birth-weight preterm infants and those who had been normal-birth-weight full-term infants (controls).^a

Variable	Controls (n = 45)	VLBWPIs (n = 48)	p
Age, years	10.23 ± 1.27	10.18 ± 1.39	0.860
Height, cm	141.72 ± 10.29	138.53 ± 11.29	0.159
Height-for-age, Z score	-0.10 ± 1.08	0.13 ± 1.22	0.323
Weight, kg	37.64 ± 9.95	34.66 ± 10.36	0.161
Weight-for-age, Z score	-0.03 ± 0.89	0.27 ± 1.02	0.123
BMI, kg/m ²	18.49 ± 3.42	17.71 ± 3.32	0.260
BMI-for-age, Z score	-0.38 ± 1.15	-0.30 ± 1.27	0.740

VLBWPIs: very-low-birth-weight preterm infants. ^aValues expressed as mean ± SD.

Table 3. Comparison of lung function variables between the schoolchildren who had been very-low-birth-weight preterm infants and those who had been normal-birth-weight full-term infants (controls).^a

Spirometric variable	Controls (n = 45)	VLBWPIs (n = 48)	p
FEV ₁ , L	2.23 ± 0.52	2.03 ± 0.59	0.092
FEV ₁ , Z score	0.71 ± 1.12	0.40 ± 1.62	0.284
FVC, L	2.59 ± 0.61	2.38 ± 0.66	0.121
FVC, Z score	0.83 ± 1.03	0.66 ± 1.44	0.525
FEV ₁ /FVC, L	0.86 ± 0.58	0.85 ± 0.89	0.498
FEV ₁ /FVC, Z score	-0.23 ± 0.95	-0.38 ± 1.13	0.507
FEF _{25-75%} , L	2.60 ± 0.74	2.36 ± 0.77	0.139
FEF _{25-75%} , Z score	-0.69 ± 1.04	-0.14 ± 1.37	0.392

VLBWPIs: very-low-birth-weight preterm infants. ^aValues expressed as mean ± SD.

Table 4. Association of perinatal and neonatal variables with lung function in the schoolchildren who had been very-low-birth-weight preterm infants (univariate analysis).

Variable	FEV ₁	FVC	FEF _{25-75%}
Birth weight	0.139	0.526	0.066
Length of hospital stay	0.336	0.996	0.164
Gestational age	0.071	0.136	0.274
PROM	0.138	0.079	0.252
Surfactant use	0.214	0.472	0.200
Duration of oxygen therapy, days	0.165	0.456	0.279
Mechanical ventilation	0.155	0.143	0.669
CPAP	0.324	0.377	0.454
HMD	0.548	0.730	0.415
Corticosteroid use	0.406	0.499	0.484

PROM: premature rupture of membranes; CPAP: continuous positive airway pressure; and HMD: hyaline membrane disease.

DISCUSSION

In the present study, the schoolchildren who had been VLBW preterm infants and those who had been NBW full-term infants were found to be similar in terms of growth (weight and height) and lung function. In addition, the schoolchildren in the VLBWPI group were found to be slightly more active than those in the control group.

Previous studies evaluating the growth of VLBW infants from discharge to early adulthood have shown that such monitoring plays an important role in identifying growth deficits and their consequences.^(11,12) Some of the aforementioned studies have shown that low birth weight is a risk factor for growth and BMI deficits.^(11,24) However, it has been reported that genetic factors

and socioeconomic status have a greater influence on growth in schoolchildren than does low birth weight.⁽²⁵⁾ These findings are consistent with those of the present study, in which schoolchildren who had been VLBW preterm infants and those who had been NBW full-term infants were found to have similar anthropometric characteristics and nutritional status.

Although prematurity and the interventions that follow from it can affect respiratory system development,⁽⁹⁾ the present study showed no evidence of reduced lung function nearly a decade later in the schoolchildren in the VLBWPI group when compared with those in the control group. These results are consistent with those of previous studies showing preserved lung function^(5,6) in schoolchildren and adults who had been low-birth-weight preterm infants. One of the most

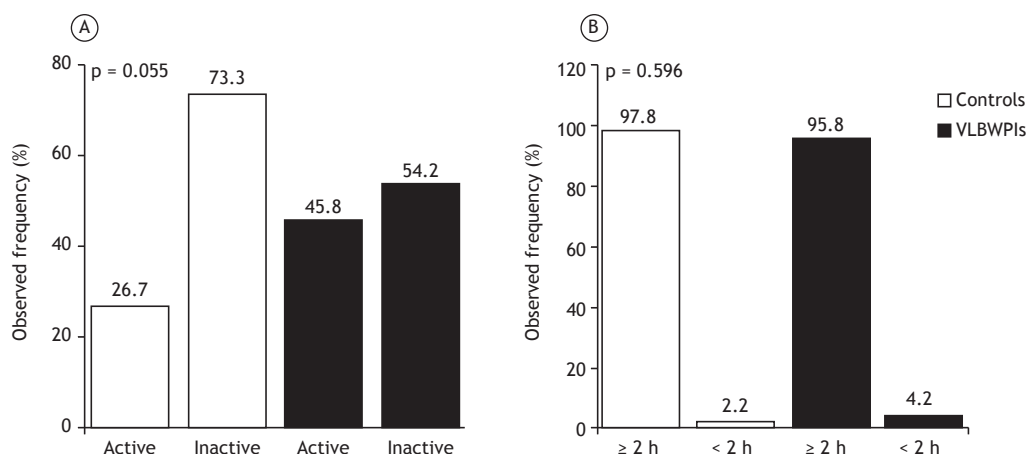


Figure 2. Comparison of physical activity level (in A) and daily screen time (sedentary behavior; in B) between the schoolchildren who had been normal-birth-weight full-term infants (controls) and those who had been very-low-birth-weight preterm infants (VLBWPIs).

compelling hypotheses to explain that is that pulmonary changes are more apparent in the first years of life and less so during childhood because parents provide respiratory health care, periodically monitoring lung function and being alert to any respiratory changes in their children.⁽⁷⁾ In addition, physical activity and adequate nutrition can contribute to the functional recovery of such individuals.⁽⁷⁾ Although some studies have suggested that socioeconomic and ethnic factors can influence lung function in such individuals,^(26,27) the present study did not evaluate that.

Our finding of preserved lung function is inconsistent with previous studies showing impaired lung function in schoolchildren who had been VLBW preterm infants.^(3,28,29) In a recent study, schoolchildren who had been born at a gestational age of less than 32 weeks and who had not received surfactant therapy were shown to be at an increased risk of pulmonary involvement.⁽³⁰⁾ These conflicting results can be attributed, at least in part, to differences in designs, lung evaluation methods, reference equations, prematurity definitions, and low birth weight classifications across studies.^(3,6,31) In the present study, only 6 of the schoolchildren in the VLBWPI group were found to have reduced lung function (as assessed by spirometry). This can be explained by the greater clinical severity of those 6 participants at birth; in comparison with the remaining VLBWPI group participants, they were born at a lower gestational age (< 32 weeks), had lower birth weight (< 1,200 g), had longer hospitalizations, and received supplemental oxygen for longer.

In the present study, perinatal and neonatal variables were not associated with lung function in schoolchildren. This result is in agreement with those of a recent study, in which no perinatal factor was significantly associated with respiratory function variables.⁽³²⁾ In addition, our result is similar to that of another study, in which low birth weight and gestational age were not associated with reduced lung function in schoolchildren.⁽³¹⁾ In contrast, other studies have shown

that weight and gestational age have an influence on the duration of oxygen therapy and mechanical ventilation in VLBW preterm infants.^(9,33) In the present study, the schoolchildren in the VLBWPI group had undergone oxygen therapy, mechanical ventilation, or both in the first days of life. However, a previous study has shown that any lung function abnormality in schoolchildren who have previously undergone oxygen therapy, mechanical ventilation, or both is more closely related to prematurity than to neonatal lung injury itself.⁽³⁴⁾ Previous studies conducted in our laboratory have shown that maximal expiratory flows are reduced in preterm infants⁽³⁵⁾ and remain so until the second year of life.⁽³⁶⁾ In the present study, the VLBWPI group showed no reduction in lung function. Our data suggest that lung function remains reduced until the second year of life and normalizes when the children reach school age, in parallel with a reduction in respiratory morbidity.

Given the high cost of objective assessment devices such as pedometers and accelerometers, physical activity assessment by self-report questionnaires is a viable and practical alternative for quantifying sedentary behavior among young people.⁽¹⁴⁾ In the present study, a questionnaire proposed by Hallal et al.⁽¹⁴⁾ was used. The questionnaire quantifies the time spent commuting from home to school, work, or both, as well as the time spent in leisure-time activities. Although the questionnaire has been widely used in and appears to be well understood by the pediatric population,^(14,37) it does not quantify the time spent in activities of different intensities and therefore might limit the understanding and interpretation of physical activity in such individuals.

In the present study, more than 60% of the sample was classified as inactive; according to previous studies conducted in Brazil,^(14,37) this constitutes sedentary behavior, which is a major public health problem. No significant difference was found between the VLBWPI and control groups in the present study

regarding the level of physical activity, a finding that is consistent with those of a study comparing children who had been preterm infants with those who had been full-term infants.⁽³⁸⁾ Although there were no significant differences between the two groups of children, those in the VLBWPI group were found to be slightly more active than those in the control group. This can be attributed to family factors, such as parental preferences for certain physical activities serving as encouragement for the children to engage in those activities, or to parental overprotection.⁽³⁸⁾ However, the influence of the aforementioned factors was not evaluated in the present study. More than 90% of the schoolchildren in the present study were found to spend more than 2 h per day watching television, playing video games, or using a computer. This finding appears to confirm those of national and international studies^(39,40) showing high levels of sedentary behavior in pediatric patients. Therefore, there is a need for strategic measures to combat sedentary behavior, given that sedentary behavior

in pediatric patients is a risk factor for physical inactivity in adulthood.⁽³⁹⁾

The main limitation of the present study is that our sample of VLBW preterm infants consisted of less than half of the total number of individuals available for recruitment. Most of those children were not located, resided in municipalities outside the catchment area, did not agree to participate, or died. However, we believe that the aforementioned limitation had no influence on the results obtained, given that perinatal and neonatal factors were similar between the VLBW preterm infants who were included in the present study and those who were not.

In conclusion, the schoolchildren in the VLBWPI group and those in the control group were found to be similar in terms of growth (weight and height) and lung function. In addition, the schoolchildren in the VLBWPI group were found to be slightly more active than those in the control group. Furthermore, perinatal and neonatal variables were not associated with lung function in the schoolchildren studied.

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