Assessment of nutritional status in children and adolescents with post-infectious bronchiolitis obliterans

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Abstract

Objective: To assess the nutritional status of children and adolescents with bronchiolitis obliterans and to analyze associations with clinical and nutritional factors.

Methods: The study included 57 patients. Nutritional status was assessed using z scores for weight/age, stature/age, weight/stature in children, and stature/age and body mass index percentiles in adolescents. Body composition was assessed via tricipital skin folds, subscapular skin folds, and the sum of both plus the muscular circumference of the arm; pulmonary function was also investigated in subjects over 8 years old.

Results: The high percentages of malnutrition and risk for malnutrition are noteworthy: 21.7 and 17.5%, respectively. Among children, weight/age and stature/age detected higher percentages of malnutrition (21.6 and 16.2%), while weight/stature underestimated this diagnosis. Among adolescents, body mass index detected a high percentage of malnutrition (25%) and of risk for malnutrition (20%). Body composition analysis detected 51% of patients with low muscle reserves, and the majority of patients had normal fat reserves. Compromised pulmonary function was associated with poor performance at exercise (r = 0.434; p = 0.024). Malnutrition and/or nutritional risk and low muscle reserves were significantly associated with the 6-minute walk test (p = 0.032; p = 0.030). There was no association between spirometry and the nutritional variables (p > 0.05).

Conclusion: These results emphasize the need for nutritional intervention, and suggest that, in addition to using weight and height indices for nutritional assessment, it is necessary to combine these with an analysis of body composition, so that a larger number of patients with malnutrition and/or at an increased risk for developing malnutrition may be identified and correctly managed.

J Pediatr (Rio J). 2008;84(4):323-330: Bronchiolitis obliterans, nutritional status, body composition, anthropometry, malnutrition, spirometry.

Introduction

Post-infectious bronchiolitis obliterans (BO) is a consequence of aggression to the epithelium of the lower respiratory tract. It is characterized by obstruction of the distal airways.[1] The prevalence of BO is unknown, but recent studies suggest it is on the rise.[2] In children, BO is more common during the first year of life and is often associated with acute viral bronchiolitis (AVB).[3]

Published studies about BO highlight that, as well its diagnosis, aggressive treatment for infections and oxygen therapy, an adequate nutritional plan should also be developed so that the illness can have favorable clinical evolution. Despite the

sparsity of literature stressing the specific importance of nutritional care in BO, as well as in other chronic respiratory diseases with acute energy consumption, patients require adequate energy intake. Though these needs are specific for each individual, the ultimate goal is to allow them to grow properly for their age.[2,4]

The few studies available[4-8] which describe the nutritional status of BO patients are inconsistent in their methods and do not explore the nutritional status of the individuals. However, all of them are in agreement on the attention given to the recovery and/or preservation of nutritional status in this clinical entity and on recognizing the consequences of nutritional deficit for the evolution of the disease.

The objective of this study is to assess the nutritional status of children and adolescents with BO and to analyze associations with clinical and nutritional factors.

Methods

The cross-sectional study was performed from October 2005 to May 2006 in a population consisting of children and adolescents diagnosed with BO which was followed in the outpatient ward of two hospitals (Hospital da Criança Santo Antônio and Hospital Materno Infantil Presidente Vargas, both in Porto Alegre, Brazil). The diagnosis of BO was based on the coexistence of: (1) persistent airway obstruction after an episode of acute airway obstruction disorder in a child previously healthy in its first year of life; (2) suggestive tomographic imaging, namely a mosaic pattern and/or bronchiectases; and (3) exclusion of other obstructive pulmonary diseases, such as cystic fibrosis (CF), tuberculosis, congenital malformation and human immunodeficiency virus (HIV) infection.[8,9] The study included children and adolescents ages 1 through 18 from both genders who had the necessary physical conditions for anthropometric measurement. Patients were classified as either child or adolescent, depending on their age group.[10]

Weight and stature anthropometric measurements were taken through the use of standard techniques and calibrated equipment.[11]

In children, nutritional status was determined using the following z scores: weight by age (ZPI), stature by age (ZEI) and weight by stature (ZPE). Malnutrition and/or low stature were defined as ZPE and ZEI ≤ -2Z, while obesity was defined as ZPE ≥ +2Z;[10] risk for malnutrition as ZPE ≤ -1.28Z,[12] and the tenth percentile for weight by stature;[13] and overweight as ZPE ≥ +1.28Z. Children with ZPE ranging from -1.27 to +1.27Z were considered eutrophic[12]. When more than one anthropometric index (ZPE, ZPI and ZEI) was used for classification of nutritional status, the lowest value was used in cases where there were discrepancies in the ranges used.

Among adolescents, the study analyzed ZEI and the distribution of body mass index (BMI) percentiles. ZEI was defined as < -2Z for classification as malnutrition and/or low stature. The study followed the *World Health Organization* (WHO) classification guidelines for the distribution of BMI percentiles.[10] Since the WHO classification does not include nutritional risk for malnutrition, we chose to adopt the classification suggested by Frisancho.[11] We also used self-assessment of sexual maturation stage,[14] in which teenagers were classified as prepubescent, pubescent or post-pubescent.[10]

In the ≤ 5 years-old group, the data were analyzed with the aid of the WHO Anthro application , beta version, from 02/17/06[15]; for patients over 5 years-old, the application used was Epi-Info, version 3.3.2, from 02/09/05, based on Centers for Disease Control (CDC) guidelines.[16] For BMI percentiles, we also compared them with other reference values.[17,18]

In assessing body composition, we used tricipital skinfolds (TSF), subscapular skinfolds (SSF) and the sum of both (SDCTS) for fat reserves, as well as the muscular circumference of the arm (MCA) for muscle reserves.[11] The measurement of arm circumference (AC) was performed using a Secca® inextensible tape measure, while skinfolds were measured with a Lange® caliper.

Pulmonary function was assessed for patients 8 years-old and older through the use of spirometry and 6-minute walk tests (6MWT). Spirometry was performed using a portable spirometer (SpiroDoc v.3.2, MIR, Italy®), according to ATS/ERS-2005 recommendations.[19] The parameter assessed was the percentage of the forced expiratory volume in 1 second (FEV_1).[20] The 6MWT was performed according to ATS-2002[21] recommendations. The parameters assessed were total distance run and final and initial oxygen saturation. Decreases in saturation were considered significant if the variation was ≥ 4%. Distance run was presented in terms of z score predicted (Z6MWT).[22]

Parents and/or guardians provided information regarding cultural and socioeconomic status when the patients and/or their guardians were invited to join the study. Those who accepted signed release forms giving their free and informed consent. The study was approved by the research ethics committees of the two hospitals involved, as per resolution 196.96 of the Brazilian Conselho Nacional de Saúde (National Health Council).

The data were stored in a database developed with the aid of the Statistical Package for the Social Sciences (SPSS) application, version 14.0. Results are expressed as follows: quantitative variables as mean average and standard deviation (SD) when distribution is symmetrical or as median average and interquartile range when it is asymmetrical; categorical variables as absolute and percentage frequencies. Statistical significance was set at 5% (p ≤ 0,05). Student's *t* test or analysis of variance (ANOVA) were used for comparing quantitative variables with symmetrical distribution. The Pearson chi-squared test or the Fisher exact test were used for assessing association between categorical variables. Pearson's (symmetrical distribution) or Spearman's

Table 1 - Distribution of children and adolescents with post-infectious bronchiolitis obliterans according to nutritional status categorization by z score and body mass index

Nutritional status	Age group		
	< 10 years-old* (n = 37)		
z score	ZPE*	ZPI*	ZEI*
-4 to -2	1 (2.7)	8 (21.6)	6 (16.2)
-1.9 to -1.28	5 (13.5)	3 (8.1)	6 (16.2)
-1.27 to 1.27	23 (62.2)	21 (56.8)	22 (59.5)
1.28 to 1.9	3 (8.1)	2 (5.4)	3 (8.1)
2 or more	5 (13.5)	3 (8.1)	0 (0.0)
	≥ 10 years-old* (n = 20)		
BMI Percentiles	BMI WHO	BMI CDC[+]	BMI Must et al.[18‡]
< 5	4 (20.0)	5 (25.0)	4 (20.0)
5-15	4 (20.0)	4 (20.0)	5 (25.0)
15-85	9 (45.0)	8 (40.0)	8 (40.0)
85-95	2 (10,0)	2 (10,0)	3 (15.0)
> 95	1 (5.0)	1 (5.0)	0 (0.0)
Stature/Age z score			
≤ -2		2 (10,0)	
> -2		18 (90.0)	
Classification*	< 10 years-old		≥ 10 years-old
Malnourished	7 (18.9)		5 (25.0)
Risk	6 (16.2)		4 (20.0)
Eutrophy	16 (43.2)		8 (40.0)
Overweight	3 (8.1)		2 (10,0)
Obesity	5 (13.5)		1 (5.0)

BMI CDC = body mass index by percentile CDC (2000); BMI Must et al.[18] = body mass index by percentile Must et al.[18]; BMI WHO = body mass index by percentile WHO[17]; ZEI = stature/age z score; ZPE = weight/stature z score; ZPI = weight/age z score.
* n (%).
[+] Kappa coefficient of concordance with CDC (k = 0.785), p < 0.001 and with Must et al.[18] (k = 0.735), p < 0.001.
[‡] Kappa coefficient of concordance with Must et al.18 (k = 0.803), p < 0.001.

(asymmetrical distribution) correlation tests were used for assessing associations between quantitative variables. The kappa test was used for assessing concordance between methods.

Results

Fifty-seven patients took part in the study, 40 (70.2%) of which were male and 40 (70.2%) of which were white. At the time of the assessment, the mean average age was 8.7 years-old (±4.2 years), ranging from 1.5 to 18.9 years-old. Thirty-seven (64.9%) of the 57 were younger than 10 years-old. As for the sexual maturation stage of the adolescents, seven (35%) were classified as prepubescent; eight (40%) as pubescent and five (25%) as post-pubescent. The median average in which the child first presents clinical signs of the disease (first episode of wheezing) was 5 months-old

(P25 = 3.0; P75 = 9.0 months), while the median diagnosis age was 12 months-old (P25 = 9.0; P75 = 17 months). The mean average birth weight was 3,012.7 g (±834.5 g); 11 patients (22%) had birth weights > 2,500 g and 11 patients (22%) were preterm. Socioeconomic status, measured as years of schooling of the mother and/or legal guardian, had a mean average of 6.6 years (±2.9 years), while the median *per capita* income, measured in multiples of the Brazilian minimum wage per month, was 0.52 (P25 = 0.36; P75 = 0.74).

Regarding nutritional status, 24 patients (42.1%) were found to be eutrophic, 12 (21.1%) were malnourished, 10 (17.5%) were at nutritional risk for malnutrition, five (8.8%) were overweight and six (10.5%) were obese. The data for nutritional status of children and adolescents, divided by age group, are shown in Table 1.

The data for body composition for the whole sample can be found in Table 2.

Table 2 - Distribution of sample of children and adolescents with post-infectious bronchiolitis obliterans according to classification of body composition (n = 57)

Variables	Percentiles/categorization		
Body composition	< 5	5-95	> 95
Arm circumference	27 (47.4)	28 (49.1)	2 (3.5)
Muscle reserves	< 5/low	5-5/medium	> 95/high
MCA*	29 (50.9)	27 (47.4)	1 (1.8)
Fat reserves	< 5/low	5-5/medium	> 85/excess
TSF*	7 (12.3)	39 (68.4)	11 (19.3)
SSF*	3 (5.3)	37 (64.9)	17 (29.8)
SDCTS	9 (15.8)	36 (63.2)	12 (21.0)

MCA = muscular circumference of the arm; SDCTS = sum of tricipital and subscapular skinfolds; SSF = subscapular skinfold; TSF = tricipital skinfold.
* n (%).

In analyses of the association between nutritional status and body composition, patients were divided into three groups, according to nutritional status: eutrophy, malnutrition and/or risk for malnutrition and overweight and/or obesity. For patients with low muscle reserves (according to MCA), there was significant association with malnourished/at risk patients (p = 0.002). For excess adiposity, the use of TSF and SSF shows that malnourished patients are significantly associated with low fat reserves. Overweight and obese patients have significant association with high fat reserves, as shown by the use of TSF, SSF and SDCTS. We should stress that, among eutrophic patients, eight (33.3%) had low muscle reserves and three (12.5%) had low fat reserves (p = 0.002; p = 0.001).

Thirty-two patients in total took part in pulmonary function analysis. Three (9.3%) could not perform the necessary motions for the tests (spirometry and 6MWT), while one (3.1%) showed deteriorating health conditions and could not finish them during the time period of this study. One patient showed exacerbating symptoms and could not finish the 6MWT, though he did perform spirometry. The data for nutritional status, body composition, spirometry and the 6MWT are shown in Table 3.

Whe the distance run in the 6MWT was assessed for the three groups, malnourished/risk (mean = -2.99Z; SD = 1.43), eutrophic (mean = -1.93Z; SD = 1,05) and overweight/obesity (mean = -1.99Z; SD = 0.81), there was no statistically significant difference between the three groups (p = 0.105). However, when patients were split into two groups, with group 1 consisting of malnourished and/or risk for malnutrition, while group 2 consisted of eutrophic and overweight/obesity patients, the difference was statistically significant (p = 0.032), and patients suffering from malnutrition or at risk for malnutrition had significantly lower Z6MWT scores than the other group. Analyzing the association between 6MWT and muscle reserves, we found that low muscle reserves patients had significantly lower Z6MWT that those with medium reserves (p = 0.030). Figure 1 shows that the average difference between both groups was 1 SD, both for nutritional status and for body composition.

There was significant positive statistical association between $FEV_1\%$ and the 6MWT (r = 0.434; p = 0.024), which indicates that, the smaller the $FEV_1\%$, the shorter the distance run. There was no significant association between decrease in oxygen saturation and $FEV_1\%$ and with nutritional variables (nutritional status and body composition) (p > 0.05). Pulmonary function, as assessed by $FEV_1\%$, did not show any significant association with nutritional variables either (p >0.05).

Discussion

The data collected in this study for diagnosis age and early clinical signs are similar to those found in other studies, which featured diagnosis ages ranging from 1 month-old to 3 years-old, [4,8,23] while the first respiratory signs are always seen before the age of 2[4] and the disease was most frequent among boys.[7,8,23] In this study, most of the population consisted of white children, which apparently follows the characteristics of the general population from which it was sampled.

The role of socioeconomic factors on morbidity and mortality for childhood respiratory diseases has been widely described in the literature:[24] poor socioeconomic and demographic status interferes strongly with the establishment and course of childhood diseases.[25] We should also highlight that the study features a high percentage of low *per capita* income families and low schooling mothers, which may be explained by the fact that the patients came from two public hospitals which provide tertiary care in a developing nation. Caldwell[26] presented evidences of the positive and independent effect of schooling of the mother on childhood mortality rates and

Table 3 - Distribution of general characteristics of patients with post-infectious bronchiolitis obliterans who performed pulmonary function tests

Characteristics	(n = 28)	95%CI
Nutritional status*		
Malnutrition and/or risk	12 (42.9)	24.6-61.2
Eutrophy	12 (42.9)	24.6-61.2
Overweight/Obesity	4 (14.3)	1.3-27.3
Body composition		
Muscle reserves (MCA)*		
Low	17 (60.7)	42.6-78.8
Medium	11 (39.3)	21.2-57.4
High	0 (0.0)	-
Fat reserves (SDCTS)*		
Low	2 (7.1)	0.0-16.6
Medium	20 (71.4)	54.7-88.1
High	6 (21.4)	6.2-36.6
FEV_1 Classification*		
mild OVD	5 (17.8)	3.6-32.0
moderate OVD	15 (53.5)	35.0-72.0
severe OVD	8 (28.5)	11.8-45.2
6MWT[‡] (n = 27)		
z score[†]	-2.37±1.2	-2.87 to -1.87
Distance run*	507.7±70.8	479.7-535.8
Oxygen saturation		
Initial saturation[†]	97.3±1.07	96.9-97.7
Final saturation[†]	95.3±3.3	94.0-96.7
Decrease in saturation	12 (44.4)	26.0-62.8

6MWT = 6-minute walk test; 95%CI = 95% confidence interval; FEV1 = forced expiratory volume in 1 second segundo; MCA = muscular circumference of the arm; OVD = obstructive ventilatory defect; SDCTS = sum of tricipital and subscapular skinfolds.
* n (%).
[†] Mean average ± standard deviation.
[‡] Did not finish the test = 1 (3.5%).

recognized the importance of the environment as an intervening factor for this association.

Literature on the assessment of nutritional status in BO patients is scarce, and there is no published scientific material similar to the methods used in this study. Therefore, this study can be considered pioneering in its assessment of the nutritional status and body composition of children and adolescents with BO.

The individuals in this study were followed by a multidisciplinary team whose members are always and at all times concerned with nutritional status. There was a notable incidence of malnutrition (21.1%) and risk for malnutrition (17.5%) among study participants. This scenario is probably due to the use of more sensitive criteria for the assessment of nutritional status, which used various indices for the description or classification of nutritional status (since it is known that

none is universal), as well as the morbidity secondary to BO, such as recurring infections, exacerbation episodes and frequent hospitalizations. Even without detailed nutritional diagnosis methods, or with the use of only one index, malnutrition was also a frequent finding in the few existing studies of BO.[4,5,7,8]

Mocelin et al.[7] report that, out of 19 patients ranging from 7 to 15 years-old, using ZPE, five (26.31%) presented mild malnutrition [$-2 \leq z < -1$] and one (5.2%) presented moderate malnutrition ($< -2z$), while all others were eutrophic, data points well below those found in this study, which found 21.1% malnourished patients and 17.5% at risk for malnutrition. The authors only used the weight/stature index for assessing nutritional status, which reflects a more recent compromise of growth with deeper consequences for weight and does not take into consideration the age of which individual. The latter
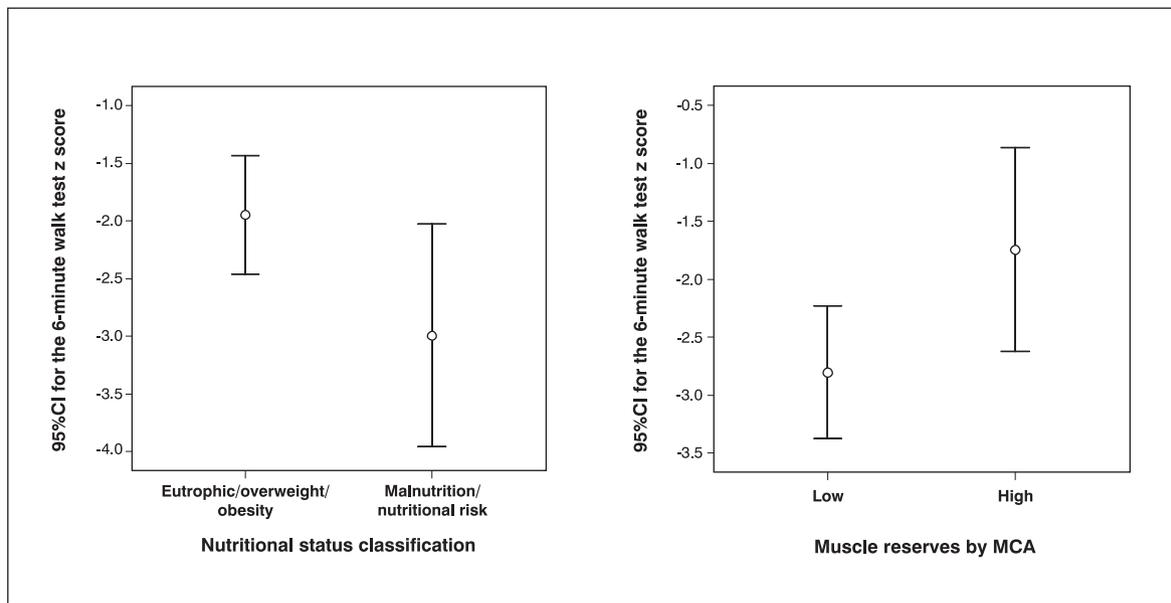
* CMA = circumference of the arm.

Figure 1 - Distribution of z score assessment of 6-minute walk test according to classification of nutritional status and muscle reserves, as per muscular circumference of the arm of patients 8 years-old or older with post-infectious bronchiolitis obliterans

index is more sensitive for the diagnosis of overweight and obesity.[10,27]

The literature does not feature reports of patients with BO who are overweight. In this study, we found 8.8% of patients were overweight and 10.5% were obese, which is similar to the values found in a study of the general population.[28]

For the indices used, among children, we found that weight/age and stature/age had higher malnutrition percentages, 21.6% and 16.2%, respectively, while weight/stature underestimated the diagnosis of malnutrition. Among adolescents, the use of BMI showed a high percentage of patients to be malnourished (25%) or at risk for malnutrition (20%). We must consider the particularities of the indices used when analyzing these results. The use of weight/age is very appropriate for tracking weight gain in children. It reflects the individual's global status, but it does not discriminate between acute and chronic nutritional compromise. Stature/age, on the other hand, expresses linear growth. The involvement of the stature/age index suggests a negative influence in child growth in the long run.[10,27,29]

For body composition, depleted muscle reserves were found in 50.9% of study patients, as estimated by the MCA, and depleted fat reserves, as estimated by TSF, SSF and SDCTS, were found in 12.3%, 5.3% and 15.8%, respectively. Fiates et al.,[30] in their analysis of the body composition of CF patients, found that 46.1% of patients had depleted muscle reserves (as estimated by assessment of MCA) and 30.7% had depleted fat reserves (as estimated by TSF). The

lack of studies of body composition in BO patients led to making comparisons with other diseases. In CF, as well as pulmonary compromise, many patients also present digestive manifestations. Therefore, these features should be taken into consideration for comparisons with BO.

Among patients classified as eutrophic, 33.3% had low muscle reserves and 12% had low fat reserves, results which highlight the need for better assessment of nutritional status, especially for patients suffering from chronic disorders. In the present study, if not for the use of wider assessment which associated weight and stature indices to body composition data, up to 45.3% of eutrophic patients, who already had some form of malnutrition (depleted muscle reserves and/or low fat reserves), would not have been properly identified and managed.

For patients (n = 28) whose pulmonary function was tested, we highlight the high percentage of individuals who were either malnourished or at risk for malnutrition (42.9%) and had low muscle reserves (60.7%). The data indicate the deterioration of their nutritional status.

Impairment of pulmonary function was found to be associated with lower performance 6MWT, a fact which can be associated with the condition of the patients, most of which suffered from moderate-to-severe chronic obstructive pulmonary disorder. Malnutrition or risk for malnutrition, as well as low muscle reserves, were significantly associated with 6MWT, which indicates the level of functional limitation for the patients. This sample allows us to infer that the deterioration

of nutritional status is directly related to performance in the 6MWT.

There was no significant association between spirometry (FEV_1%) findings and nutritional variables. We must consider that, since this is a rare disorder, only a small sample of patients performed spirometry. The population presented an important nutritional deficit. It is also relatively homogeneous in pulmonary compromise, since 82% of patients have moderate-to-severe chronic obstructive pulmonary disorder.

The data may reflect the morbidity associated with BO. It reinforces the need for multidisciplinary follow-up for these patients, similar to what happens with other pulmonary disorders, such as CF. We stress the importance of systematic nutritional assistance, as well the periodic and detailed assessment of nutritional status for these patients. Nutrition might become an important prognostic factor for BO evolution due to the importance of pulmonary growth tracking somatic growth.

In the present study, patients presented major nutritional compromise, which indicates that both impairment of pulmonary function and malnutrition are associated with lower performance levels in the 6MWT exercise. Future studies are needed to discover whether malnutrition and low muscle reserves are inherent consequences to BO or if this condition can be reverted with the use of more specific nutritional therapy.

Acknowledgements

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