Motor delay in cystic fibrosis infants: An observational study☆

Paula de Almeida Thomazinho a,⁎, Célia Regina Moutinho de Miranda Chaves b, Caroline Pinto Pássaro c, Maria Dalva Barbosa Meio a

a Pediatrics Department, Instituto Fernandes Figueira/FIOCRUZ, Rio de Janeiro, Brazil
b Nutritional Department, Instituto Fernandes Figueira/FIOCRUZ, Rio de Janeiro, Brazil
c Education Department, Postgraduated Course of Neonatal and Pediatric Physiotherapy, Instituto Fernandes Figueira/FIOCRUZ, Rio de Janeiro, Brazil

A R T I C L E   I N F O

Article history:
Received 9 February 2011
Received in revised form 30 April 2011
Accepted 28 May 2011

Keywords:
Child development
Motor skills
Cystic fibrosis
Risk factors

A B S T R A C T

Objective: To verify the prevalence of delay in gross motor development in cystic fibrosis (CF) patients.

Study design: This is a cross-sectional observational study. A total of 15 children with CF were included in the analyses. The selection criteria was age between 6 and 42 months. Data on demographic, anthropometric, clinical characteristics and severity score (Shwachman) were obtained from patient records. The Bayley Scales of Infant and Toddler Development® – III Edition (BSITD-III) was used to assess motor abilities.

Results: Motor development delay was observed in 26.7% (n = 4) of the children and, in 75% of these, there were statistically significant differences between gross and fine motor scores. Low stature, low weight and periods longer than 60 days at hospital showed statistically significant association with motor delay (p = 0.025, 0.032, 0.003, respectively).

Conclusion: The prevalence of motor delay in the studied sample was high, suggesting that biological and ambient conditions of risk present in CF contribute to early motor deficits. Thus, the observation of the motor development in these patients is important for planning an adequate intervention.

© 2011 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Children’s development can be influenced by biological and environmental factors, which can cause the individual to becoming more susceptible to changes in the acquisition of motor skills [1–5].

Cystic fibrosis (CF) is a hereditary disorder, autosomal recessive, with systemic and progressive involvement. It is the most common genetic illness considered severe [6]. Clinical signs, such as electrolytic changes in sweat, chronic obstructive lung disease, poor intestinal/bowel absorption, and malnutrition are frequently present in infancy: 47.4% of them from 1 to 6 months of age, requiring periodical hospitalizations in Brazil [7–9].

The nutritional involvement and the respiratory illness, added to the recurring need for hospitalization, at a physiological phase marked by distinctive evolutionary features, could in some way compromise the motor development of a child with CF.

Although monitoring of development is fundamental for the child’s health, as well as a guideline for other strategic health interventions [10], up to the present there is only one study with children from 4 to 6 years of age with CF focusing on aspects of motor skills development [11]. So, this is the first study to examine motor development in infants below 4 years old with CF.

The aims of this study are to describe the prevalence of delay in motor development and their association with clinical and socio-demographic characteristics of children with CF.

2. Methods

2.1. Type of study and sample selection

This is a cross-sectional observational study [12], with convenience sample of patients from Instituto Fernandes Figueira/Fundação Oswaldo Cruz/Ministry of Health-Brazil, performed between May and October 2009. All children between 6 and 42 months of age with cystic fibrosis diagnosis [13] were included. The lowest age limit was defined by the period when the clinical manifestations of the illness became more evident [8], and the upper age limit, by the requirement of the instrument used for the development evaluation. Hospitalized children or children with perinatal hypoxia or asphyxia, low weight at birth (<2500 g), prematurity, presence of malformation and congenital infection, genetic syndromes and neurological and sensorial involvement (visual and/or hearing deficits) were excluded, in total of four patients.

☆ The authors declare no conflicts of interest.

⁎ Corresponding author at: Setor de Fisioterapia Motora, Departamento de Pediatric, Instituto Fernandes Figueira/FIOCRUZ, Av Rui Barbosa, 716-Flamengo, CEP 22250-020 Rio de Janeiro RJ, Brazil, Tel.: +55 21 2554 1771.

E-mail address: ptthomazinho@iff.fiocruz.br (P. de Almeida Thomazinho).
2.2. Clinical, sociodemographic and motor developmental evaluation

Age at diagnosis and at onset of clinical treatment were obtained, as well as frequency, period and cause of the hospitalizations, respiratory and digestive manifestations, bacteriology and severity of illness, based on the Shwachman-Kulczycki score (SS) [14].

Classification of the nutritional state was determined according to the Nutrition Consensus for cystic fibrosis [15] using the World Health Organization (WHO) reference curves [16], in the AnthroPlus 1.0.2. software. The weight-for-age index (W/A), though not recommended by this consensus, was evaluated according to its importance to the children below 2 years of age [1, 17]. The low index weight-for-age was determined as W/A below percentile 3 [16]. For assessment of body composition, the length of the mid-upper arm muscle circumference (MUAMC) was used [18]. Socio-economic data (schooling and per capita family income) were obtained with the parents/guardians.

The Motor Scale of the Bayley Scale of Infant and Toddler Development®, Third Edition (BSITD-III) [19] was used for the assessment of motor development from 0 to 42 months. This instrument consists of 138 items (66 dealing with fine motor skill and 72 with gross motor skill) and its application was performed according to the recommendations of the manual and by a qualified psychologist, blind to the clinical conditions of the children.

The BSITD-III is a reliable and valid test procedure for motor performance assessment, with a high test–retest stability (r ≥ 0.80) and reliability (r = 0.91 for motor composite score; r = 0.98 for gross motor subtest in risk infants) [19, 20].

Gross and scaled scores of each child were obtained from the observation and recording of their motor skills, considering their chronological age and the standardized sample (n = 1700). Critical values ≥ 3 points among the scaled scores were considered significant, according to the instructions in the manual. The sum of these last constituted the composite score for the classification of motor development delay, with cutoff point of 85 [19].

The evaluation was performed soon after medical examination, with the objective of controlling for any variable of confusion (such as stress and fatigue). The children should be clinically stable, without acute respiratory or digestive exacerbation.

In case of detection of any motor abnormality, the assessment was repeated, with a maximum interval of 3 weeks, so as not to influence the scores previously obtained. The best performance was used for the data analysis.

The occurrence of physiotherapy motor treatment, previous to the evaluation, or concurrent to it, its duration and if it was home care assistance, were investigated.

2.3. Statistical analysis

The Epi Info 2008 version 3.5.1 program was used for statistical calculations. Values of mean, median, percentile, standard deviation and absolute frequency were used for descriptive analysis. The Fisher Exact Test was used for comparison of categorical variables; and the Mann–Whitney and Kruskall–Wallis non-parametric tests for testing differences in continuous measurements, with significance levels set at 0.05. The charts were drawn with the Microsoft Office Excel, 2007.

This study was approved by the Ethics Committee for Research in Human Beings — CEP/IFF (no. FR254230-21/05/2009). All the parents or guardians of the children signed a free and informed term of consent.

3. Results

3.1. Clinical and sociodemographic characteristics

A total of 15 patients were assessed, ten (66.6%) male and five (33.3%) female, with mean of 24.7 (± 9.8) months of age. There was no statistically significant difference between the mean age of boys and girls (p > 0.05).

Schooling shorter than or equal to four years was observed in approximately 20% of the parents, with a per capita family income of up to 0.5 of the minimum salary in 60% of the families.

The mean age at the diagnosis and at the onset of clinical treatment was 6.8 months (± 4.16) and varied from 3 to 16 months, and in 46.7% it was started during the first four months. Exocrine pancreatic insufficiency was observed in 80% of the patients. All sample presented respiratory manifestations. The SS showed that, concerning general activity, 85.7% of the sample had excellent score. The SS showed that 85.7% of the sample had excellent general activity score. Regarding the physical examination score, the indexes were excellent or good in 69.2% of the children, and fair or regular in the remaining ones; as to the nutritional score, 92.9% achieved excellent or good levels, with only one with regular record.

The higher frequency of hospitalizations occurred during their first year of life, with 11 children (73.3%) hospitalized. The median period of hospital permanence in the first year was 38 days (0–85 days), and two children (13.3%) were hospitalized for more than 260 days. After their first year of life, only six children (42.9%) needed hospitalization again. A maximum period of 33 days was verified in 66.6% of the cases (n = 4), but two children have been hospitalized for more than 183 days, if the uninterrupted and discontinuous hospitalization periods were added.

The means and medians of hospitalization periods related to groups of bacteria did not show statistically significant differences, though this distribution was not homogeneous.

Fig. 1 shows the total punctuation of the SS and the comparative analysis with the total hospitalization period during their first year of life and the following ones.

The patients' nutritional state, evaluated with the criteria of the nutritional consensus in cystic fibrosis, identified malnutrition in 6.66% (n = 1) of the cases, nutritional risk in 19.98% (n = 3), nutritional adequacy in 73.36% (n = 11) and low stature in 46.7% (n = 7). Low weight (W/A < p3) was found in 26.7% of the sample (n = 4). Body composition was calculated in only nine children, owing to difficulties in augmenting the MUAMC and the tricipital cutaneous fold, and identified malnutrition was present in 44.4% of the children (n = 4).

3.2. Motor development

Motor development delay was identified in 26.7% (n = 4) of the children studied. In these cases, the two assessments of BSITD-III presented scores with equivalent confidence intervals. Fig. 2 shows the distribution of the composite scores for motor evaluation, with the linear trend line of that.

![Fig. 1. Presentation of the hospitalization length and disease severity score (Shwachman Score) by patient.](image-url)
Previous physiotherapy intervention was found in 50% ($n=2$) of the children with motor delay, and in 18.2% ($n=2$) of those with adequate motor development for their age.

Gross motor (GM) performance was below the expected for their age, as well as the fine motor performance, in 10 children (66.7%), based on the correlation values of the manual scale; this difference was higher than the limits of normal variation (1–3 points) in four of them. The disparity between the chronological and motor ages varied from 7 to 9 months. A single record was identified with a significantly greater discrepancy for GM (6.66% of the whole sample).

It wasn’t observed any abnormalities of tone while resting, or an abnormal persistence of primitive reflexes. The altered functional characteristics were: acquisition of the sitting posture with and without support, of gait without support, moving from prone or four supports to standing posture without support, walk backwards, run, kick balls, jump from a step, jump forwards, go up and down stairs without support, walk over a straight line, and interrupt running when asked to. In one child it was found asymmetrical in the acquisition of the static balance on a single foot at 34 months.

Concerning the contribution of gross motor performance for motor development delay, there was a tendency for this outcome only when the differences among the motor subscales were significant (≥3 points) ($p=0.07$).

Low weight (W/A < p3) and low stature (S/A < p5) showed statistically significant results for the outcome of motor delay ($p<0.05$) and low amplitude motor performance. Among children classified with nutritional risk ($n=3$), 66.25% presented motor development delay. Among those with adequate nutritional state ($n=11$), this prevalence was 18.2%. All the children with motor delay had longer permanence in hospital during their first year of life (85–310 days). The correlation between hospitalization and motor delay was statistically significant for periods longer than 60 days ($p=0.003$). There was a tendency for statistical correlation between the lowest values of SS score and motor delay (Table 1).

There was no statistically significant difference between the means of age at beginning of treatment and per capita family income of the children with motor delay and those with typical motor development.

**4. Discussion**

The prevalence of motor abnormality in this study was high, compared to the general population (14%) [1,2,12,22], but similar to that observed in children with low gestational age, which is an already established condition of risk for motor development [23]. It should be noted that this prevalence could be higher, considering that 18.2% ($n=2$) of the children with adequate motor development for their age had received motor physiotherapy intervention.

In the sample studied, it was observed that the mean ages at the moment of the diagnosis and the beginning of treatment were compatible with those found in the developed countries [24], but lower than other Brazilian studies [9,31]. This can reflect a higher severity of the disease of these patients, or improvement in the knowledge of the disease, both among population and health professionals, or in the therapeutic care itself.

A greater involvement of gross motor development was found, in relation to fine motor development, in all several age groups. The gross motor skills with the highest records of delay concerned the deficits of the dynamic and static postural control, especially orthostatism, and the eccentric muscular strength of lower limb. According to Shumway-Cook and Woollacott [25], these facts could be explained by the greater complexity of circuits involved for the progression and body stability, in the tasks of mobility and locomotion assessed, that include, besides changes in the musculoskeletal system, the development or building up of answering synergies, used for keeping balance, and the development of adaptive and anticipatory mechanisms, when compared to the manipulation of objects in a static position.

In spite of the limitations inherent to the outlining of the study, the analysis of the motor scores distribution chart also suggests, among the children with adequate performance, a tendency for the low mean of motor development score, discreetly decreasing with the increase of their age. Since the variability in the motor acquisitions among the age groups decreases after their first year of life, some ‘catch up’ of motor skill should be possible in later phases. According to Gruber and colleagues [11], this can also suggest a greater influence of the disease on the first years of life, followed by some recovery at school age, and later deterioration with the clinical evolution of the disease. Longitudinal studies can clarify this question.

As to gender, there was no difference in the motor delay. According to Papalia and Olds [26], boys and girls tend to have equivalent motor development in their first two years of life, being more different in the social and personality development. These findings were confirmed.
by the multicentric study with healthy children of the same age, performed in five countries from different continents [27]. Nevertheless, there are indications of influence of gender in motor performance of older children and adolescents [28].

The malnutrition prevalence observed in this study varied according to the criterion used for classification: anthropometric indexes of the Nutrition Consensus or body composition. Among the children evaluated as malnourished by the last criterion (26.4%), only one showed agreement with the anthropometric indexes; the remaining ones were classified as eutrophic (n = 2) or at nutritional risk (n = 1). Chaves and colleagues [29], studying cystic fibrosis patients from 6 to 18 years old, observed that changes in their body composition can precede the decrease in their weight and stature. This is a relevant result because the decrease in the lean mass could justify the consequences on gross motor development and a hypothetical reduction of muscle strength.

Low weight and stature were significantly associated with the outcome of motor delay. This demonstrates that the adequate nutritional support in infancy is essential for the development, as this period is very important for nervous system organization, with a high growth rate and functional acquisitions. In the child with CF this is an added risk, due to the higher energetic demand inherent to the physiopathological characteristics of the disease [8,9]. The prevalence (26.7%) of low body weight (W/A < p3) was similar to the one described by other authors [30]. However, the low stature found (46.7%) was greater than that in other studies with Brazilians and North American children (15-19.6%, 31.25%) [29,31,32]. The family genetic potential, or the presence of the ΔF508 mutation, or the association of both, could contribute to this finding, but the absence of data about it, as it was not the objective of this study, does not allow us to affirm so. In any case, it is an important data, because severe and prolonged malnutrition is frequently associated with development delay [33,34].

Concerning the use of the Shwachman severity score, the highest values were not used, since the radiological criterion was not applied, because the radiographic examinations had varied in regularity or had been performed previously to the evaluations. Despite this limitation, there was a tendency for statistical correlation between the lowest values of this score and motor delay. This correlation is expected, given the complex consequence of the disease.

A high prevalence of hospitalization was observed in the patients’ first year of life (73.3%) and hospitalization periods longer than 60 days showed a positive association for motor delay. This result is worrying because, according to Miranda and colleagues [35], prolonged hospitalization reduces the opportunities for movement and interferes in the initial motor acquisitions. Lenke [36] also demonstrated delay in head and trunk control in children who were immobilized for a long time or who showed any respiratory involvement.

Some authors demonstrate the influence of external stimulus in the systematic changes of motor development because they compromise the normal functioning of the neural systems during their critical period, in which the axons are competing for synaptic sites [3,37].

In addition, the motivation of the child for the exploration of and interaction with its sociocultural environment is essential for its motor acquisitions. According to Mello [38], the social isolation of the malnourished could be more important than the direct influence of the lack of nutrients in the development of the CNS, in relation to its impact on the child’s behavior, for social isolation reduces its social interactions, activity level, exploratory behavior and attention. Thus, permanence in favorable surroundings influences normal development and offers higher potentials of exploration and interaction. Even if malnutrition is overcome, the child suffers a slowing of its learning process, presenting gaps in its long-term development [39].

After prolonged and critical conditions of disease, the muscular ability to generate strength is also affected by the presence of pro-inflammatory mediators, such as the tumoral necrosis factor (TNF-α), as well as the alteration in the distribution of electrolytes (potassium, sodium and chlorine), which reduces the rest potential of the muscular membrane [40].

Besides the biological risk, the majority of children in this study belonged to low per capita income families. The socio economical level is mentioned as a risk for the development delay, including the cognitive development [20,41]. The family income can be considered an important factor in the child’s health conditions, owing to its influence on the possibility of the acquisition and use of essential goods and services [42]. Although was found no correlation with motor delay and income per capita in this study.

As regards schooling, there was a greater prevalence of motor delay among the children whose mothers had less than four-year schooling. The social economic variable correlates not only with problems of feeding, clothing, room, furniture, hygiene, but also with certain parents’ behaviors, such as absence of intellectual and cultural stimulation of the child, or a general reduction in the continuity and variability of social stimulation. This is confirmed by the study of Andrade and colleagues [41], which showed a positive association of the mother’s schooling level with the quality of the environmental stimulation received by the child.

Thus, the vulnerability situations found may have their etiology related to many factors, as presented in the ‘transactional model’ of development by Sameroff and Chandler [1], which considers development as the final outcome of risk and protection factors, reinforcing the multifactorial characteristic of development. According to these findings, other studies have demonstrated that both biological and socioenvironmental factors of risk of alteration in the development are associated to adverse consequences [4,5,43].

Though it is part of a cohort of patients from a regional reference center of cystic fibrosis’ treatment, the small number of participants is a limitation of this study. Hence, hierarchical regression analysis could not be performed. Studies with larger samples of patients might show different results.

5. Conclusion

The high prevalence of motor abnormality detected suggests that the risk factors associated to cystic fibrosis can, in fact, cause repercussions in motor acquisitions. The results point to possible losses in previous stages of motor development, during its critical period, either for paucity of adequate experimentation or for deficit in the recruitment of muscular units and for development of the motor skill, which deserve a more detailed investigation.

Hospitalization, prevalence of malnutrition according to stature/age and weight/age have proved to be significantly associated to motor delay in this study, reinforcing the multifactor feature of development and the concept cumulative effect of risk.

In this way, the knowledge of the initial consequences of the disease in motor development should be extended, and the planning of early physiotherapy strategies should be well founded in order to minimize future musculoskeletal dysfunctions, common to these patients.

Conflict of Interest statement

None declared.

References
