Mental performance of very low birth weight preterm infants: assessment of stability in the first two years of life and factors associated with mental performance

Desempenho mental de bebês pré-termo de muito baixo peso ao nascer: avaliação da estabilidade nos dois primeiros anos de vida e fatores associados ao desempenho mental

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Abstract

The aim of this study was to investigate the stability of mental performance of very low birth weight premature infants during the first two years of life, and to identify factors associated with mental performance.The study included 109 children. The Mental Scale of Bayley Scales of Infant Development – Second Edition was administered at 6, 12 and 18-24 months of corrected age. The stability of the scores between assessments was verified by the analysis of variance for repeated measures. The association of the major social and neonatal characteristics with mental development was confirmed using multivariate analysis by linear regression, considering the following outcomes: mental development indices at 6 months, 12 months and between 18-24 months of corrected age. The mean Mental Developmental Index (MDI) was 83.4 (SD: 12.4) at 6 months, 86.4 (SD: 13.9) at 12 months, and 73.4 (SD: 14.5) at 18-24 months. A significant decrease in the mental developmental index (13 points) at 18-24 month corrected age was observed. The Mental development index did not show stability during the first two years of life in this population of preterm infants, except for children with neonatal pneumonia whose performance was unsatisfactory in all assessments. Among the risk factors investigated only male gender and neonatal pneumonia were associated with outcomes.

Keywords: Child development. Premature. Cognition. Follow-up studies. Infant. Psychomotor performance.

Resumo

O objetivo do estudo foi investigar a estabilidade do desempenho mental de bebês prematuros de muito baixo peso ao nascer ao longo dos dois primeiros anos de vida e identificar os fatores associados ao seu desempenho mental. Estudo de coorte com 109 crianças. A Escala Mental da Bayley Scales of Infant Development – Second Edition foi aplicada aos 6, aos 12 e entre 18-24 meses de idade corrigida. A estabilidade dos escores entre as avaliações foi investigada através de análise de variância para medidas repetidas. A associação entre as características neonatais e sociais no desenvolvimento mental foi verificada por análise multivariada através de regressão linear, considerando como desfechos os Índices de Desenvolvimento Mental aos 6 meses, 12 meses e entre 18-24 meses de idade corrigida. A média do Índice de Desenvolvimento Mental aos 6 meses foi 83,4 (DP: 12,4), aos 12 meses foi 86,4 (DP: 13,9) e aos 18-24 meses foi 73,4 (DP: 14,5). Observou-se uma diminuição significativa de 13 pontos no escore aos 18-24 meses de idade corrigida. O Índice de Desenvolvimento Mental não apresentou estabilidade ao longo dos dois primeiros anos de vida nesta população de prematuros, exceto para as crianças que tiveram pneumonia neonatal, cujo desempenho foi insatisfatório em todas as avaliações. Dos fatores de risco investigados, apenas o sexo masculino e a pneumonia neonatal estiveram associados aos desfechos.

Palavras-chave: Desenvolvimento infantil. Prematuro. Cognição. Seguimentos. Lactente. Desempenho psicomotor.

Introduction

Growth and development are some of the concerns faced by parents and professionals who take care of preterm infants. The scientific and technological advances combined with the changes occurred in perinatal care have contributed to increase survival of newborns with increasingly reduced weight[1]. The increased survival rate of infants with ever more reduced gestational age draws greater interest concerning the influence of prematurity on child development, leading to increasing research about the uniqueness of this population. Biological risks, including organic immaturity, use of respirator, bronchopulmonary dysplasia, cerebral hemorrhage, septicemia, among others, and the socioeconomic and environmental conditions determine the prognosis of children born prematurely concerning their mental and motor development after birth[2,3]. Family income, family support, and maternal education are important factors that influence the development[4].

Preterm infants with very low birth weight are more likely to develop cognitive and behavioral problems[5-9]. The dynamic characteristic of the development of premature babies, due to malleability of the neuropsychomotor development, calls for serial evaluations in the first years of life [3,10]. The variability in mental performance was also observed in high-risk children, regardless of the gestational age, which reinforces the need for this follow-up [11-13].

There was a poor correlation among the results obtained from an assessment on the mental performance stability of a group including preterm infants, carried out in the first and second years of life. The authors suggest that specific high-risk groups may have different performances over two years, and that future research must be directed to other groups of children at high risk to provide information studies about development and to early intervention programs. [14]

Given the dynamics of development, this paper suggests that there is stability

in mental performance over the first two years in premature infants, especially in high- risk groups.

The purpose of this study was to assess mental performance stability in infants with very low birth weight in the Bayley Scale of Infant Development over the first two years of life and to identify factors associated with this performance at 6, 12, and 18-24 months .

Methods

A hospital-based prospective cohort study was held including 303 premature infants (gestational age less than 37 weeks) with very low birth weight (less than 1500 grams) born between January 2004 and January 2008. The infants were hospitalized in the Neonatal Intensive Care Unit and monitored in the Outpatient Clinic for Monitoring Newborns under Risk, and assessed for their development.

The study excluded 68 newborn infants with genetic syndromes or congenital malformations or infections, and 59 deaths in neonatal period. Moreover, it excluded four post-neonatal deaths and four children with bilateral blindness diagnosed in this period. Therefore, the total population under evaluation was composed of 167 children.

The Bayley Scale[15] was applied to 139 children at 6 months old, to 126 children at 12 months old, and to 117 children between 18 and 24 months corrected age. The difference between the number of children in the initial population and the number of children who underwent the development test at certain ages is due to failure to attend appointments to perform the test. This study only considered children who completed the three assessments of development (at 6, 12, and between 18 and 24 months corrected age), and due to this criterion the population under study consisted of 109 children.

The neonatal and social characteristics of the children in the study were compared with those of loss group, and there were no statistically significant differences between them, suggesting the absence of selection bias.

All children received outpatient pediatric follow-up every month up to 12 months of corrected age, and every three months from 13 to 24 months. On the same day of the routine medical examination previously scheduled, the Bayley Scales of Infant Development-Second Edition (BSID-II)[15] were applied by two trained psychologists, at 6, 12, and between 18 and 24 months corrected age. This study considered the BSID-II Mental Scale only, which is composed of 178 items (distributed in patterns according to age in months), which assess memory, habituation, problem solving, primitive concepts of numbers, generalizations, classification, vocalizations, language, and social skills. The performance achieved by the child in the BSID-II was measured using the Mental Development Index (MDI). The mean of this index is 100 and the standard deviation is 15. According to the scores obtained, the performance is classified as normal if equal or greater than 85, moderate delay if between 70 and 84, and serious delay if below 70. The psychologists who applied the scale were unaware of the children's clinical history, but they were aware that they were premature with very low birth weight. The interobserver reliability (between the two psychologists) measured by the intraclass correlation coefficient (ICC) was 0.94 (CI: 0.80 to 0.98).

Although Bayley Scales are considered the gold standard in assessing development in children up to 42 months, they were not standardized for the Brazilian population or to high-risk children. The performance classification recommended by the scale author and used in this study was a result from the standardization for the American population of low risk. Due to the need to compare it with other studies and lack of standardized scales for our population in this age group, we chose to classify the performance as proposed by the scale's author (normal, moderate delay, and serious delay), though cross-cultural differences are considered.

To describe the mental performance evolution, all index values of the mental

development were converted for the performance rating (normal, moderate delay, severe delay) proposed by author of the scale[15]. Children with regular performance scored Mental Development Index equal or above 85, those with moderate delay scored MDI between 70 and 84, and those with severe delay scored below 70.

The following information were collected in the hospitalization period, and they were obtained by consulting hospital records and interviews with the infants' mothers: a) maternal data: age, number of pregnancies, parity, last menstrual period, estimated gestational age by obstetric ultrasonography conducted before 20 weeks gestation, obstetric complications, number of prenatal appointments, and use of antenatal corticosteroids; b) neonatal: sex, gestational age at birth (by somatic and neurological characteristics of the newborn), birth weight, type of delivery, Apgar scores, use of tracheal intubation in delivery room, resuscitation procedures, use of mechanical ventilation, duration of oxygen therapy, use of surfactant, patent ductus arteriosus, hyaline membrane disease, neonatal pneumonia, septicemia, use of oxygen therapy for over 28 days (bronchopulmonary dysplasia)[16], and use of oxygen therapy with 36 weeks of corrected age (moderate/severe bronchopulmonary dysplasia) [16], peri-intraventricular hemorrhage, leukomalacia, hospitalization period. After release from the Neonatal Unit, the study obtained information about breastfeeding and social characteristics: family income, maternal education, father interaction, and daycare attendance.

The gestational age was estimated by last menstrual period, or in case of uncertainty about this date, by the obstetrical ultrasound performed up to 20 weeks of gestation. In the absence of both, the gestational age considered was the one obtained by the method described by Ballard[17], which consists in the assessment of the somatic features and neurological evaluation of the newborn. The classification of weight adjustment to the gestational age was based on Alexander's intrauterine growth curve [18], which was considered small for the gestational age (SGA) when the birth weight was below the 10th percentile for gestational age, and infants born weighing between 10 and 90 percentiles were considered appropriate for the gestational age (AGA). The diagnosis of peri-intraventricular hemorrhage was obtained by serial cranial ultrasound exams up to 40 weeks of corrected age. The study considered light levels of hemorrhage (1 and 2) and severe ones (3 and 4), according to Papile's classification[19]. The septicemia was considered in the presence of positive blood cultures. The corrected age was calculated by subtracting, from the chronological age, the number of weeks missing necessary for the child to reach the term (40 weeks of gestational age).

A sample size of 109 children was estimated to detect an 8 points difference in the Bayley Scale between male and female children, assuming a standard deviation of 15 points, α=0.05, and power = 0.80.

Data analysis

The data were analyzed using STATA 10 (Stata Corp, 2007)[20] and SPSS (SPSS for Windows, Inc, Chicago, Illinois, USA). The description of the main features of the population was made by frequency measures, mean, median, and standard deviation. The study calculated the prevalence of change in the Mental Development Index (MDI) at 6, 12, and 18 to 24 months of corrected age.

Comparisons were made to investigate the stability among MDI means in the three periods assessment using analysis of variance for repeated measures. The stability in the MDI was considered when there was no statistically significant difference among the averages in the three moments.

To compare the proportions according to the classification of altered and normal performance between 6 to 12 months, 12 and 24 months, and 6 and 24 months, the study used the Cochran's Q test. To identify among which age the differences could be observed in the assessments, the study

performed the nonparametric McNemar test for dependent samples.

To verify the association of the main neonatal and social characteristics of mental development, the study conducted linear regression analysis considering as outcomes the Mental Development Index at 6 months, 12 months, and between 18-24 months of corrected age. The independent variables selected were those that presented p <0.20 in the bivariate analysis. The Stepwise strategy was used in the multivariate analysis to select the variables, and the level of significance for the Forward procedure was of 0.05, and for Backward procedure was 0.10. In the final model, the level of significance was 0.05.

Results

The mean maternal age was 26 years old (SD = 7.0), and the maternal schooling level was 8 years of study for the 109 newborns studied. The mean household income was 988 Brazilian real. The antenatal corticosteroid therapy was used by 94% of these mothers. Table 1 presents the main characteristics of the population studied. The children remained hospitalized for an average period of 60 days.

The mean age of children in the first application of the Bayley Scale was 6.5 months (SD = 0.89), 12.6 months (SD = 1.08) in the second application, 23.2 months in the third one (SD = 3.32).

The mean Mental Development Index (MDI) at 6 months was 83.4 (SD: 12.4), at 12 months was 86.4 (SD = 13.9). The assessment carried out between 18-24 months of corrected age showed a decrease of 10 and 13 points, respectively, in the mental performance and a significant difference when compared to previous assessments. There were also differences in MDI means in the first two years of life for all subgroups analyzed, except for the subgroup of 13 children with neonatal pneumonia, who showed poor performance in the three assessments. Even for the subgroup of children without the risk factors analyzed, which are female and with no neonatal morbidity, there were differences in the

Table 1 - Characteristics of very low birth weight infants included in the study, born between 2004 and 2008 (n = 109).

Tabela 1 *- Características da população de prematuros de muito baixo peso incluídos no estudo nascidos entre 2004 e 2008 (n =109).*

Male sex - n (%)	51 (46.8)
Cesarean section n (%)	73 (67)
Tracheal intubation - delivery room - n (%)	39 (36)
Gestational age (weeks) - mean (SD)	29 (2)
Birth weight (g) - (SD)	1122 (240)
Hyaline membrane disease, n (%)	83 (76.1)
Use of surfactant - n (%)	59 (54)
Neonatal pneumonia - n (%)	13 (11.9)
Ventilatory assistance n (%)	63 (57.8)
Period of oxygen therapy (days) (median)	11
Bronchopulmonary dysplasia - n (%)	38 (34.9)
Moderate/Severe Dbp - n (%)	17 (15.6)
Septicemia - n (%)	16 (14.6)
Peri-intraventricular hemorrhage - n (%)	25 (22.9)
Leukomalacia - n (%)	1 (0.9)
Patent Ductus Arteriosus, n (%)	55 (50.5)
Smal for Gestionational Age - n (%)	45 (41.3)
Weighting below 1000grams - (%)	30 (27.5)
Gestionational age below 28 weeks - n(%)	27 (24.8)

Table 2 - Comparison of mean Mental Development Index (IDM) from 6 months to 18-24 months corrected age according to neonatal characteristics.

Tabela 2 *- Comparação de médias do Índice de Desenvolvimento Mental (IDM) dos 6 meses aos 18-24 meses de idade corrigida segundo as características neonatais.*

	IDM 6 months Mean [SD]	IDM 12 months Mean [SD]	IDM 18-24 months Mean [SD]
Total Population			
Population w/o risk factor	88.6 [8.9]	94.0 [12.5]	73.9 [14.2]*
Sex			
male	80.4 [13.3]	80.6 [13.4]	68.5 [13.6]*
female	86.1 [10.9]	91.6 [12.5]	77.7 [13.8]*
DBP			
With DBP	79.8 [14.8]	81.6 [15.1]	72.8 [16.1]*
Without DBP	85.3 [10.5]	89.0 [12.7]	73.7 [13.5]*
Neonatal pneumonia			
With pneumonia	70.9 [17.3]	70.5 [10.7]	65.7 [13.3]NS
Without pneumonia	85.1 [10.6]	88.6 [13.0]	74.4 [14.3]*
Birth weight			
PN<1000g	78.2 [14.5]	81.1 [14.7]	73.1 [16.7]*
PN ≥ 1000g	85.4 [10.9]	88.4 [13.2]	73.5 [13.5]*
Gestational age			
IG< 28s	81.4 [14.3]	82.2 [14.7]	73.5 [14.9]*
IG≥ 28 s	84.1 [11.4]	87.8 [13.6]	73.3 [14.3]*
HPIV			
With HPIV	80.1 [16.0]	82.8 [16.6]	69.2 [14.3]*
Without HPIV	84.4 [11.0]	87.8 [13.6]	73.3 [14.3]*
Adequacy PN-IG			
PIG	83.6 [8.8]	88.5 [11.6]	73.9 [13.5]*
AIG	83.3 [14.3]	85.0 [15.3]	73.0 [15.0]*

Analysis of variance for repeated measurements at 6m, 12m and 18-24m: *p<0.001 NS - non significant

*Análise de variância para medidas repetidas aos 6m, 12m e 18-24m: *p<0,001 NS - não significativo*

DBP - bronchopulmonary dysplasia; PN - Birth weight; IG - gestational age; HPIV - peri-intraventricular hemorrhage; PIG - Small for gestational age; AIG - Appropriate for gestational age

DBP - Displasia broncopulmonar; PN - Peso de nascimento; IG - Idade gestacional; HPIV - hemorragia peri-intraventricular; PIG - Pequeno para a idade gestacional; AIG - Adequado para a idade gestacional

MDI means. Therefore, there was no stability of MDI over time for most very low birth weight preterm infants. The mean MDI of the total population and of subgroups at 18-24 months ranged from 65.7 to 77.7 (Table 2).

In the unadjusted model, boys showed worse performance than girls did at 6 and 12 and 18-24 months. Children with bronchopulmonary dysplasia (BPD) showed the worst performance at 6 and 12 months compared to those without BPD. The same was true when comparing the performance of those with birth weight below and above 1000g. Children with neonatal pneumonia showed low mental performance in the three ages, and this difference was significant for the three ages compared to children who did not show such pathology (Table 3).

Fifty-five percent of children underwent breastfeeding with milk formula supplementation and the average time of mixed milk feeding was 4 months. At 24 months, the mean MDI of children who were breastfed was 72.6 (SD: 14.2), and those not breastfed 69.9 (SD = 14.7) (p = 0.35). There were also no significant differences in relation to means IDM at different ages evaluated when analyzing mother's education, living with the father, and day care attendance (data not shown in the table).

In the multivariate analyzes conducted with outcomes the Mental Development Index, the study found out that at 6 months of age, the association with the outcome took place with the neonatal pneumonia variable. At 12 months of age, the association was with neonatal pneumonia and male sex. At 18-24 months of corrected age, the association occurred only with the male sex variable (Table 3).

The MDI results converted to the mental performance classification are shown in Table 4, with a significant increase in the frequency of children with delay in the last assessment. To make this comparison, the study considered the grouping of moderate delay and severe delays. There was significant difference between the proportions of abnormal tests in the three ages assessed. The comparison of proportions of children with delays at 6 months and 18-24 months, and children at 12 months with 18-24 months showed significant statistically difference.

The assessments over the two years corrected age showed two groups of results in relation to performance. A group of children (n = 34) remained stable, as they kept the same classification of development in three the ratings: 19 (17.4%) remained under regular performance since the first assessment, 7 (6.4 %) remained under moderate delay, and 8 (7.3%) with serious delay since the first evaluation. Therefore, 75 (68.8%) of the children showed change in the mental performance classification.

Tabela 3 - Modelo de regressão linear entre variáveis demográficas e neonatais e o Índice de Desenvolvimento Mental aos 6 meses, 12 meses e entre 18 e 24 meses de idade corrigida.
***Table 3** - Linear regression model between demographic and neonatal variables and the Mental Development Index at 6 months, 12 months and between 18 and 24 months corrected age.*

	Model gross not adjusted		**Final model adjusted**	
At 6 months	**β**	**p**	**β**	**p**
Bronchopulmonary dysplasia	-5.50	0.026	-0.83	0.76
Brain hemorrage	-4.31	0.12	-1.57	0.57
Gestational age <28s	2.6	0.34		
Smal for Gestionational Age	0.33	0.89		
Birth Weight <1000g	-7.13	0.006	-4.49	0.08
Neonatal Pneumonia	-14.10	0.00006	**-11.22**	**0.003**
Male Sex	-5.73	0.014	-3.93	0.09
At 12 months				
Bronchopulmonary dysplasia	-7.4	0.007	0.64	0.84
Brain hemorrage	-4.65	0.14	-1.59	0.59
Gestational age <28s	-5.68	0.067	-0.64	0.85
Smal for Gestionational Age	3.5	0.19	1.9	0.47
Birth Weight <1000g	-7.34	0.013	-4.23	0.17
Neonatal Pneumonia	-18.12	0.000	**-13.19**	**0.002**
Male Sex	-10.96	0.000	**-8.77**	**0.000**
At 18-24 months				
Bronchopulmonary dysplasia	-0.82	0.77		
Brain hemorrage	-5.4	0.09	-4.56	0.15
Gestational age <28s	-0.18	0.95		
Smal for Gestionational Age	0.9	0.74		
Birth Weight <1000g	0.33	0.91		
Neonatal Pneumonia	-8.7	0.039	-4.61	0.27
Male Sex	-9.2	0.001	**-8.5**	**0.002**

All models were applied using corrected ages / *Todos os modelos foram aplicados utilizando-se a idade corrigida*
$r^2_{6\ months} = 0.19$; $r^2_{12\ months} = 0.29$; $r^2_{18\text{-}24\ montns} = 0.14$ / $r^2_{6\ meses} = 0,19$; $r^2_{12\ meses} = 0,29$; $r^2_{18\text{-}24\ meses} = 0,14$

Table 4 - Classification of mental performance obtained at 6, 12 and 18-24 months corrected age in the population of very low birth weight infants.
Tabela 4 *- Classificação do desempenho mental obtido aos 6, 12 e 18-24 meses de idade corrigida na população de prematuros de muito baixo peso.*

	6 months	12 months	18-24 months
Normal-n (%)	60 (55.0)	64 (58.7)	26 (23.9)
Delay - n (%)	49 (45.0)‡	45 (41.3)**	83 (76.1)*
Moderate delay - n (%)	36 (33.0)	32 (29.3)	38 (34.9)
Severe delay - n(%)	13 (12.0)	13 (12.0)	45 (41.2)

Delay- moderate and significant delay categories were grouped
‡ Cochran Q test: p < 0.0001 (6 months x 12 months x 18-24 months)
* Mc Nemar test: p = 0.0001 (6 months x 18-24 months)
** Mc Nemar test: p = 0.0001 (12 months x 18-24 months)
Atraso- As categorias atraso moderado e atraso grave foram agrupadas
‡ teste Cochran Q: p < 0,0001 (6 meses x 12 meses x 18-24 meses)
** teste Mc Nemar: p=0,0001 (6meses x 18-24 meses)*
*** teste Mc Nemar: p=0,0001 (12 meses x 18-24 meses)*

It is noteworthy the increase in the percentage of children with delay in the third assessment. Out of 49 children with abnormal performance (moderate and severe delays) at 6 months, after reaching 24 months, 45 of them were still classified as having developmental delay.

Discussion

There was no stability in this studied population, if comparing the MDI means in the assessments held in the first two years of life, even for those subgroups of children that showed no neonatal morbidities. Moreover, the majority (76.1%) of the children reached, at 18-24 months, indexes lower than 85 in the mental development assessment using the Bayley Scale. In the adjusted analysis, only the sex was associated with the outcome, showing a worse performance for boys, with an 8.5 MDI average difference. Between 18-24 months, mean MDI values for all subgroups were below the cutoff of "normality" defined for infants born at term and of low risk. About two thirds of the group showed a change in the classification of development in the assessments, mainly due to a tendency of worse performance of children classified as having "normal development" at 6 months, if compared with the results at 18-24 months.

In Brazil, there is little academic research on mental performance along time of preterm infants[13,21]. Few international studies were conducted to investigate the stability of this population concerning mental performance[11,14,22].

Bayley Scales assess each stage development level and their main feature is to enable the diagnosis of developmental delay and enable the planning of intervention strategies[15].The measure of stability in repeated assessments is important to assess the progress of these children. Upon detecting any abnormality in the exam/test, the team that assists children in this study provides guidance to the relatives concerning the stimulation toward the cognitive, motor, and behavioral areas. The team also sends them to proper therapies. However, at two years old, the index obtained were still poor.

As mentioned before, there is not a standard scale for the Brazilian population or to preterm infants, so the results that classify mental performance must be interpreted with caution, as cross-cultural aspects may influence the attributes considered to classify the "normal development". The application of the Bayley Scale enables to compare the assessment of children' performance along time with other studies. The use of corrected age by two years is one of the recommended measures for partially minimize the effect of prematurity,

approaching the development of preterm children to term. However, this study cannot state that adopting the cutoff used by the standardized scale for American children to term is appropriate for premature infants. Therefore, the possibility to have an "abnormal" overestimated frequency of performance is not ruled out.

The purpose of this study was not to assess the predictive value of the Bayley Scale, but to know the development pattern of the population studied along the first two years of life, using the mental performance dynamics in this scale. The BSID-II manual states that, over time, there is high correlation between the scores of children considered normal, but the manual does not include studies for high-risk populations[15]. The author reports that a two point increase is expected in the Scale score as age increases. These results reflect the stability in relation to children considered at low-risk, and are accordingly to the work of Harris et al.[22] These authors reported a MDI increase from the first to the second assessment in children at low-risk (95 to 100.8). Still, with high-risk children, the reverse occurred, as the MDI decreased in the first assessment at 7 months for the second assessment at 18 months (85.7 to 82.3).

The stability of the Bayley Scales of children with Down syndrome and children with clinical problems (44% preterm infants), referred to an early intervention program, was evaluated in the first and second years of life. The correlation between these assessments using the BSID-II was considered moderate for the group with Down syndrome (r = 0.65), and poor for the second group (r = 0.37)[14]. The authors suggest that specific high-risk groups may have different performances over two years, and that future research must be directed to other high-risk children groups to provide information to studies about development and to early intervention programs.

Most studies detects a reduction of mean scores in the population of children with birth weight below 2000 g[23], preterm and extremely low birth weight children[24], with high risk[11] (use of drugs during prenatal or perinatal complications), or with HPIV[12], assessed by the Bayley Scale, either in the comparison of first year with the second[11,12], or of second year with third year[24]. The deterioration of mental performance tends to be greater as greater the risk in prenatal and neonatal periods [11], which may also be associated with lower weight[25]. Regarding the MDI value, there was an average decrease of 10 points [11, 12]. In our study, the occurrence of neonatal pneumonia showed similar results on the mental index, but it seems that this impact is more important in the first year of life.

In this study, the comparison of group of children weighing less than 1000 grams with those weighting higher showed a greater change in the Bayley Scale scores, with a declining tendency for both groups. The group with extremely low birth weight (weight<1000grams) showed a performance classified as delay since the first assessment compared to the group weighing more than 1000g, which showed such delay only in the third assessment, a finding similar to another study[24].

Moreover, the lack of stability was mainly due to the significant decrease in the third assessment score (18-24 months), which suggests a cognitive function worsening of high-risk infants studied in this age group. There was a 13 points reduction in mental performance at 18-24 months corrected age, partly explained by the greater complexity of tasks performed in this age. Among the items analyzed, those related to language seem to be among the most affected ones in these premature infants, which possibly has a greater impact in the reduction of the mental development index.

Concerning the comparison between boys and girls, boys' history of mental development is more regular than girls, and a predictive ability of development at 6 months in relation to development at 18 and 36 months, not reported for girls[25]. This difference was due to the fact that areas of language are more accelerated in girls than in boys. One explanation would be the sex

related genetic difference in the ability of the expressive language and that genetic, biological, and environmental factors may contribute to differences between boys and girls in language development[25]. In this study, among characteristics investigated such as factors associated with MDI, the male sex was the variable that remained associated in older ages after controlling for confounding variables.

There was no association between environmental and social factors and cognitive impairment in this population. This differs from literature: association between the highest level of maternal education and higher scores in intelligence tests[12], and higher scores in assessments using BSID-II.[26] Hack *et al.*[27] observed that at two years of age, the environmental influences become more apparent and a critical transition begins to work with the development of skills related to symbolic functions, language development, and early formation of concept. Environmental factors that could be associated with mental performance were not included in this model, such as the stimulation of the child by the legal guardians, providing toys, organization of a supportive environment, and parental practices and styles.[28]

Although there was a decline in performance observed in this study and in most studies with infants at risk, Procianoy *et al.*[21] reached different results by comparing two groups of Brazilian children born with very low birth weight (one appropriate for gestational age and another small for gestational age), assessed with the BSID-II at 8, 12, 18, and 24 months corrected age. Both groups showed an increase in MDI scores from 8 to 24 months of corrected age, and in the last assessment, half of the population obtained a score classified as normal. This indicates a need for broader studies with premature infants in Brazil, investigating the characteristics of such delay for a better understanding of which it may be associated to. However, it is important to note that in this study, the majority (91.8%) of children with moderate and severe delays in the first assessment kept this level of performance over time, suggesting that the test results at 6 months may be useful to indicate early intervention.

Study Constraints

In the cohort study, many children did not attend the three recommended assessments, but the social and neonatal characteristics of children from the loss group did not differ from children who remained in the study.

Bayley Scales are considered the gold standard [11] to assess the development, but have not been standardized for the Brazilian population yet, or to children born prematurely. Although several studies in the country apply this scale, the findings cannot be generalized to the Brazilian population, due to differences in relation to the U.S. population, where the scale was standardized. In this study, the result refers to a population at high risk and lower socioeconomic status, assisted in a public hospital of reference for fetal risk, so it cannot be generalized to the general population of newborns with very low weight.

The use of instruments is essential for mental development assessment. In Brazil, there is a notable lack of updated and standardized instruments that have been tested, translated, and adapted to our reality[29].

Conclusion

For the premature infants with very low birth weight studied, the Mental Development Index in the three ages did not show stability, so there was a worse performance at 18-24 months. Except for the subgroup with neonatal pneumonia, whose MDI average remained stable with poor performance in the three assessments. The male children were most affected in the last two ages assessed.

Although the Bayley Scale is not standardized for the Brazilian or high risk population, the stability analysis of the mental index can be performed, as the

comparisons were made by observing the means MDI of the same group of preterm infants at different ages. This study cannot assure that the performance rating used as normal/abnormal is appropriate, facing cross-cultural aspects and characteristics peculiar to preterm infants.

Accurate measures of child development in children at risk are necessary for early identification and intervention, so actions can be developed to guide families on how to stimulate the infants, sending them to specialized therapies to minimize the consequences of premature birth.

Ethical matters

This work is part of a longitudinal, prospective study, approved by the Ethics Committee of Instituto Fernandes Figueira in 2004, and it was renovated in 2006 (CAAE 0066.0.008.000-03/ 0005.0.008.000-06). The legal guardians responsible for the children who participated in the cohort study signed an informed consent.

We declare that this work was free from connection or financing agreement between authors and companies or individuals who may have interests in the material discussed in this paper.

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