Risk factors for language development associated with prematurity

Variáveis de risco para o desenvolvimento da linguagem associadas à prematuridade

Ana Cláudia Constant Soares[1], Kelly da Silva[2], Patrícia Aparecida Zuanetti[3]

ABSTRACT

Introduction: This study relates prematurity to linguistic impairments. **Purpose:** To analyze several variables related to prematurity, identifying the risk factors for language development disorders. **Methods:** Medical records of 98 preterm-born children (1 to 6 years) were analyzed. Data on language development (DENVER II test) and several variables, such as gestational age, length of hospital stay and postnatal complications were collected. From the Denver II test results, the sample was divided into two groups: G1: 28 children with risk factors for linguistic impairment; G2: 70 children without risk factors for linguistic impairment. Regression models and Fisher test ($\alpha=0,05$) were used for statistical inferences. **Results:** The presence of peri-intraventricular hemorrhage (PIVH) or bronchopulmonary dysplasia (BPD), maternal age less than 18 years, birth weight less than 1000g and long hospital stay were identified as risk factors for language development. There was also an association between risk for language disorders and the presence of risk in motor and social areas. **Conclusion:** Prematurity itself cannot be assigned as a risk factor for language development. In such cases, the variables associated with prematurity must be further assessed, limiting the involved risk factors. In this study, the presence of PIVH, BPD, maternal age less than 18 years, birth weight less than 1000 grams and long hospital stay were identified as risk factors for language development.

Keywords: Infant, Premature; Risk factors; Child language; Language development; Language disorders; Neurodevelopmental disorders

RESUMO

Introdução: Estudos relacionam a prematuridade a alterações linguísticas. **Objetivo:** Analisar as diversas variáveis relacionadas à prematuridade, identificando os fatores de risco para alteração no desenvolvimento linguístico. **Métodos:** Foram analisados 98 prontuários de crianças nascidas pré-termo (1 a 6 anos). Coletaram-se dados referentes ao desenvolvimento de linguagem (teste Denver II) e dados referentes a diversas variáveis, tais como idade gestacional, tempo de internação e intercorrências pós-natal. A partir do resultado no teste Denver II, dividiu-se a amostra em dois grupos: G1: 28 crianças com risco para alteração linguística; G2: 70 crianças sem risco para alteração linguística. Para as inferências estatísticas, utilizou-se modelos de regressão logística e teste Fisher ($\alpha=0,05$). **Resultados:** Foram identificadas como fatores de risco para o desenvolvimento da linguagem as variáveis presença de hemorragia peri-intraventricular (HPIV) ou broncodisplasia pulmonar (DPB), idade materna inferior a 18 anos, peso ao nascimento inferior a 1000g e longo tempo de internação. Também houve associação entre risco para alterações de linguagem com a presença de risco nas áreas motoras e social. **Conclusão:** A prematuridade, por si só, não constitui um fator de risco para o desenvolvimento de linguagem. Nesses casos, é necessário investigar melhor as variáveis envolvidas na prematuridade, delimitando os fatores de risco envolvidos. Neste estudo, a presença de HPIV e peso inferior a 1000 gramas, ao nascer, foram identificados como principais fatores de risco para o desenvolvimento de linguagem, seguidos pelas variáveis DPB, longo tempo de internação e idade materna inferior a 18 anos, no momento da gestação.

Palavras-chave: Recém-nascido prematuro; Fatores de risco; Linguagem infantil; Desenvolvimento de linguagem; Transtornos da linguagem; Transtornos do neurodesenvolvimento

INTRODUCTION

Language acquisition depends on a neurobiological and social apparatus, i.e., on the integrity of all brain structures, an adequate cognitive functioning, social interaction and the quality of stimuli that the child receives from its environment. Damage to any of these aspects may specifically affect language skills, which develops in parallel and integrally / intrinsically with cognitive skills[1]. This development may be affected by several complications during gestational, perinatal and / or postnatal periods, among which prematurity is one of the known risk factors for linguistic impairment[1,2,3,4,5,6,7,8,9,10,11].

According to the World Health Organization[12], newborns are babies with a gestational age of less than 37 completed weeks (borderline preterm infants: 35-36 gestational weeks; moderate preterm infants: 31-34 gestational weeks; extremely preterm infants: <30 gestational weeks) given that, the lower the gestational age, the greater the probability of mortality, abandonment and health problems.

In Brazil, according to a multicenter study in 2014, the overall mean rate of prematurity is 12.3%[13]. In recent years, technological advances have led to an increased number of neonatal intensive care units and to the development of their medical care, contributing to the reduction in mortality of preterm infants, even in extremely preterm or low weight infants[14]. These changes have led to an increase in the number of children in need of monitoring the development.

The difference of neurological development between preterm and full-term infants can be assessed in an objective way and at an early age by means of brain magnetic resonance imaging, in which different patterns of brain activity are observed, showing delayed maturation of several brain regions[15], and the assessment of brainstem auditory evoked potentials[16,17], which are considered early physiological markers, indicating which children may have language development disorders in the future[16]. Behavioral tests / scales are also widely used to assess and monitor the neuropsychomotor and linguistic development of preterm infants in tertiary referral hospitals, enabling early detection of changes.

Regarding the linguistic development of this risk group, there are evidences that preterm infants have changes in several linguistic subdomains[5,6,8] and those changes are variable, i.e., a child may have impairments in phonological development, but not in lexical development[18].

There are reports in the literature involving the population of preterm infants pointing out that impairments in expressive language are more frequent when compared to those of receptive language[10,11] and that, between 2 and 3 years of age, pragmatic disorders, characterized by a difficulty in the heuristic function and in respecting communicative turns, participating and maintaining dialogic activities, are observed[9]. At preschool age, phonological disorders and difficulties with narratives prevail[10].

Prematurity is undoubtedly a risk factor for neuropsychomotor and linguistic development, but clinical practice associated with results of a few studies[8,19] has shown that the risk for development does not originate from prematurity per se, but from its relation to several complications resulting from this condition (e.g., weight, gestational age, perinatal events).

The knowledge about which variables are most commonly related to delays or impairments in language development is extremely important. From this knowledge, more attention could be paid to children who present such variables, by means of more detailed assessments, aiming at the diagnosis of language disorders and inclusion in therapeutic programs, as early as possible, in order to minimize future losses.

This study aimed to analyze several variables related to the condition of prematurity (maternal variables, conditions at birth and postnatal conditions), identifying which of them are risk factors for language disorder.

METHODS

Ethical considerations and sample selection

This study was approved by the Research Ethics Committee of the Clinical Hospital of the Ribeirão Preto Medical School, *Universidade de São Paulo* under the number 9416/2015. There was no need to sign the informed Consent Form by those responsible for the participants, as this was a longitudinal study, yet retrospective, where the data collected were in the electronic and printed medical records of the subjects.

A total of 120 medical records of preterm infants (gestational age at birth less than 37 completed weeks) were analyzed, followed up at outpatient clinics of a specialized tertiary referral hospital for premature infants. Data from the electronic and printed medical records of the infants, who had medical follow-up in these outpatient clinics, were obtained from October 2014 to March 2015. In these outpatient clinics, the patients are followed up by a multiprofessional team and there are periodic evaluations of children's neuropsychomotor development using the Denver II scale.

After analyzing the medical records, the children were divided into two groups, according to the results obtained in the Denver II test for the language area: Group 1 (G1) - preterm infants with risk factors for language delay and Group 2 (G2) - preterm infants without risk factors.

The following inclusion criteria were considered: children born preterm (gestational age at birth less than 37 completed weeks) and followed up at specific outpatient clinics; children whose physical and/or electronic medical records contained all the information required by the protocol used in this study; for G1 - preterm infants with unsatisfactory results in one or more Denver II tests (the change in the test could have occurred at any time of the child's age, so the

"impaired" classification was not mandatory as the last result of the Denver II test performed on that child) and, for G2, preterm infants with satisfactory results in the test. Children with diagnosed genetic syndromes, presence of hearing loss or encephalopathies due to prenatal or perinatal event were excluded.

At the end of the study, data from 22 children were excluded and the total sample consisted of data from 98 children. Among those, 28 children were classified as G1 (13 female and 15 male) and 70 children as G2 (32 female and 38 male).

Material and procedures for data collection

The printed and electronic medical records of the selected patients were consulted. The information collected were related to pregnancy, birth data, conditions of the child at birth, conditions and procedures performed in the postnatal period, as well as information regarding the results obtained by the application of the Denver II test (Chart 1).

The Denver II test[20] is an assessment scale used by many health professionals that can be applied to children from birth

Chart 1. Variables collected from medical records

Identification data	Birth date
	Current age
	Gender
Maternal variables	Maternal age at birth
	Use of drugs or alcohol during pregnancy
	Diseases or complications during pregnancy
	Prenatal care (number of medical appointments)
	Type of delivery
Conditions at birth	Gestational age
	Birth weight
	Size for gestational age
	Apgar score at 1 and 5 minutes
Posnatal conditions	Presence of neonatal jaundice
	Presence of peri-intraventricular hemorrhage
	Presence of bronchopulmonary dysplasia
	Presence of seizures
	Length of hospital stay (Total, in ICU and NICU)
	Need for O2 support
	Other diseases or postnatal complications
Denver II results	Presence of risk factor for language
	Presence of risk factor in another area of Denver II
	Age at which the risk factor was identified in Denver II
	Conduct adopted after identification of risk factors for language

Subtitle: ICU = Intensive Care Unit; NICU = Neonatal Intensive Care Unit; O2 = Oxygen

to 6 years. It consists of 125 tasks related to four areas of development (personal-social, language, fine motor adaptive and gross motor). The information can be obtained in two ways: through direct observation or report of the primary caregiver, being that for each item, answers regarding its performance can be classified as "normal" (when the child performs the item according to what is expected for its age); "caution" (when the child fails or refuses to perform the task at an age when 75% to 90% of the children do it) and "delayed" (when there is failure or refusal to perform a task executed by more than 90% of children of the same age). Children can be classified as having a "normal" (when there are no delays and a maximum of one caution), or "suspect" development (when there are two or more cautions and / or one or more delays) [20]. It is worth mentioning that the classification is given for each assessed area and it is possible for one child to be at risk for language delay and to have appropriate performance in other areas.

Statistical analysis

Methods of descriptive statistics were used to characterize the groups. Regression models and Fisher test (α=0.05) were used for statistical inferences.

One of the goals of the logistic regression is to identify risk factors and protective factors for prematurity / language impairment. Initially, all independent variables were analyzed for their association to the risk of language impairment in the Denver II test. The logistic regression model associated with the Stepwise method was used to identify among all variables analyzed which were, in fact, risk factors. Each step of the stepwise method consists in including a new independent variable in the model and verify its significance, or removing a variable from the current model if no longer significant, according to some predetermined criterion. Here, only the independent variables at a significance level of 0.1 (α=10%) and gestational age, for example, were selected to integrate the final logistic regression model. In the final model, a significance level of 0.05 (α=5%) was used. For the design of this model, all variables were transformed to categorical variables.

The Fisher's exact test found an association between risk for language development and risk in another area assessed in the Denver II test.

RESULTS

The age of the children ranged from 2 to 6 years. It was observed that 14 children of G1 became a "risk" classification in the Denver II test between the first and the third year of life; 5 children whose age of identification was less than 1 year and 3 children whose age of identification was above 3 years had the same classification.

Among all the variables studied, those which were most related to risk for language were selected using an initial logistic regression model, considering all the independent variables available combined with the Stepwise method, with significance level of α=10% for the inclusion or exclusion of variables from the model. The "weight" ("positive" - risk factors / "negative" - protective factors) specifies the association between the variable "language impairment" and the considered independent variable. The "weight" was calculated by statistical analysis (Table 1).

Table 1. Results of the multivariate logistic regression model combined with the Stepwise method for variables related to birth and posnatal conditions (α=0.10) – initial model

Variable	Statistical weight
Maternal age at birth (<18 years)	Positive
Maternal age at birth (18-30 years)	Negative
Gestational age (<28 weeks)	Positive
Birth weight (<1000g)	Positive
Birth weight (>1000g)	Negative
Peri-intraventricular hemorrhage	Positive
Total length of hospital stay (15-30 days)	Negative
ICU length of hospital stay (more than 15 days)	Positive
NICU length of hospital stay (15-30 days)	Negative
Bronchopulmonary dysplasia	Positive
Anemia	Negative

Subtitle: ICU = Intensive Care Unit; NICU = Neonatal Intensive Care Unit
Note: Positive weight = risk factor (when the characteristic is present, the chance of the child having linguistic disorders is bigger); Negative weight = protective risk factor (when the characteristic is present, the chance of the child having linguistic disorders is lower)

After selecting the variables described in Table 1, a new logistic regression model was developed (now considering only the variables in Table 1), combined with the Stepwise method, with a significance level established at 5% (Table 2).

Table 2. Results of the multivariate logistic regression model combined with the Stepwise method for variables related to birth and posnatal conditions (α=0.05) model

Variable	Weight	p-value
Maternal age at birth (18-30 years)	-1.0245	<0.01297*
Birth weight (>1000g)	-1.5458	<0.00226*
Peri-intraventricular hemorrhage	1.2448	<0.0088*
ICU length of hospital stay (<15 days)	0.8464	<0.01100*

* Significant values (α=0.05) – Logistic regression model combined with the Stepwise method.
Subtitle: ICU = Intensive Care Unit
Note: Estimated negative value = protective factor; Estimated positive value = risk factor

It was further observed that the presence of risk factor for

language impairment was associated with risks to the fine motor (p<0.01), gross motor (p<0.01) and personal social areas (p<0.01).

In 9 cases, according to Denver II test, information about the approach adopted by health professionals after identification of the risk factor for language disorders were not found in the medical records. Seven children were referred for speech-language pathology evaluation at this institution and 6 children already underwent speech-language pathology follow-up at the institution, in their cities of origin or at an integrated rehabilitation center.

DISCUSSION

Prematurity is considered an important risk factor for neuropsychomotor and language development. A number of studies in the field of child development have investigated the association between preterm birth and handicap in this development, comprising sensory, growth, language and / or learning gaps[2,3,4,5,6,7,8,9,10,11].

However, such risk is not due to prematurity per se, but can be attributed to the adverse conditions associated with preterm birth, which may evolve to nervous system damage[5,8,19,21,22]. The aim of this study was to assess the adversities to which children born under the complex condition of prematurity are exposed, determining which factors are involved in the language development delay.

In the present study, the age at which the prevalence of risk in the language area was identified was between 1 and 3 years. According to the literature, language disorders in preterm infants are more evident by 6 months of age[6], since at this stage, the critical period of brain development takes place, when the neurogenesis, gliogenesis, neuronal migration and myelination processes occur at high speed[23]. Regarding the linguistic question, the transition from the preverbal to the verbal period is observed in this age group and, thus, delays are more easily identified by relatives and / or other health professionals of other areas than speech, language and hearing sciences.

In the sample of this study, a greater percentage of children classified as extremely preterm infants (less than 28 weeks) were observed, because the data collection site is a tertiary referral hospital, i. e., it aims to meet the demand of medical care that requires high technology equipments and highly specialized training team. In the first model of this study, extreme prematurity was considered an important risk factor to be analyzed, since it causes a long period of hospital stay and several perinatal events. The reason for this is that, in the last gestational trimester (from 24 weeks onwards), the critical period for brain development[23] and the first "neuronal pruning" begins, which may lead to a brain reorganization in children born at this stage.

Birth weight was also considered an important factor

and weight less than 1000 g was related to the increased chance of language development disorder. The literature has shown this influence of low birth weight on the linguistic development[2,5,8,19,24,25].

Peri-intraventricular hemorrhage (PIVH) and bronchopulmonary dysplasia (BPD) were also related to linguistic delay, however, BPD had a smaller impact than HPIV. The literature indicated that PIVH is a common neurological disease in preterm newborns, especially in those weighting less than 1500g. This event happens due to the fragile morphology of the brain region where this type of hemorrhage occurs (region of neuronal proliferation and origin of brain support tissue) and to the high vascularization of that region[26]. The literature has shown that the presence of PIVH in the perinatal period, especially in the most severe cases (grades II, III and IV), was associated with central auditory disorders[17] and motor[8] and language delays[8,27].

In the first logistic regression model of this study, BPD was identified as a risk factor for language development. Although, in the final logistic regression model, this variable does not demonstrate statistical significance, studies have already shown that BPD may have impact on development, associating with cognitive impairments[8,19]. There were also reports that children who progressed with BPD had deficit in intelligence, reading, mathematics and fine motor skills, when compared to those born full-term and premature without BPD[28].

Considering that language acquisition depends on the association between neurobiological and social apparatuses, being the latter related to the social interaction and quality of stimuli received in the child's environment[1], variables related to maternal characteristics may interfere in the proper language development. If these maternal characteristics, such as age at the time of pregnancy and level of education are already of utmost importance for the linguistic development of full-term infants[29], analyzing them in infants born preterm is even more necessary.

This study identified that maternal age was considered as a risk or protective factor for impairment of language development. In the first statistical model of logistic regression, it was observed that maternal age under 18 years was a risk factor and maternal age between 18 and 30 years was a protective factor, being the latter statistically significant in the second model of logistic regression applied.

In a study with mothers of preterm infants with low educational level, lower socioeconomic status and some with maternal age of 18 years[19], it was observed that they had no knowledge about child development, only noticing motor impairments and not the cognitive impairments in their children. When mothers reported about the development of their children, they used words and terms spoken by health professionals, failing to understand the meaning of those words. However, another study[30] stated that when parents receive information about child development and guidance on how to stimulate their child, whether or not they participate in oriented counseling programs, preterm infants tend to improve their development.

Another finding in this study was the correlation between the presence of language impairment and the presence of impairments in other areas, such as motor and social development. This result is in agreement with the literature, which states that preterm infants are more prone to developmental delays in motor, linguistic and cognitive areas[5,8], i.e., developmental delays in general, causing negative consequences for the child's adaptation and socialization process.

These information reinforce the need for these children to be followed by multiprofessional teams so that their development is observed as a whole and not in a fragmented way or in isolated areas. It is important to reflect on the issue of "early multidisciplinary interventions" as, considering that the sample of this study came from a tertiary referral hospital and that children were followed up to 6 years in specific prematurity outpatient clinics, there was a considerable rate of children who presented a risk for language impairment and were not referred for evaluation or speech-language pathology intervention.

Another important factor is that the Denver II test is a scale which follows the development of language, but does not assess in detail the pragmatic, phonological, morphosyntactic and semantic aspects, thus it is important, in case of mother's or school's complaint regarding language and speech, refer the child for a specific evaluation, even in the presence of a "without risk" classification on global development scales.

It is necessary to advise teachers, parents and other health professionals that language disorders should be identified at an early stage, thus preventing future problems, such as difficulties in written language development[4].

CONCLUSION

Prematurity in itself cannot be assigned as a risk factor for language development. The presence of PIVH and birth weight less than 1000 grams were the variables related to prematurity considered as risk factors for linguistic development. Other variables, such as BPD and long length of hospital stay should also be considered, however, their association with the risk of language delay was weaker. Furthermore, social factors, such as maternal age at the time of pregnancy less than 18 years, contributed to the increase in language difficulties. It was also often to find motor and social difficulties and problems related to the adaptive behavior among children who presented changes in language development.

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