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Andes pediatr. 2022;93(4):535-542
DOI: 10.32641/andespediatr.v93i4.4107

ORIGINAL ARTICLE

Psychomotor development trajectories according to nutritional status in breastfed children

Trayectoria del desarrollo psicomotor según estado nutricional en niños alimentados con lactancia materna

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Received: October 27, 2021; Approved: March 10, 2022

What do we know about the subject matter of this study?

Psychomotor development in breastfed infants may be better than in those who have not been breastfed; in addition, it is known that overweight increases the probability of having lower psychomotor test scores compared with eutrophic infants.

What does this study contribute to what is already known?

In eutrophic or overweight breastfed children, the trajectories of nutritional status and psychomotor development are stable and within normal ranges. Knowing the developmental trajectories will allow establishing specific reference curves for each developmental domain.

Abstract

Objective: To describe psychomotor development (PMD) trajectories and nutrition in children fed with breastfeeding (BF) and to evaluate possible associations. **Subjects and Method:** Prospective cohort of full-term infants, without known pathologies, fed with BF. The intake of BF was evaluated with an isotopic technique at three months. At six successive ages, the nutritional status was evaluated according to the body mass index (BMI) for age and the PMD using the Ages and Stages Questionnaire (ASQ-3). Children who had at least two follow-up evaluations were included. Multivariate analysis of the trajectories by the PMD domain was performed according to BMI/A and BF, controlled by bio-socio-demographic variables. **Results:** 53 children were included (60% male), 76 % were eutrophic, and 62% and 38% were fed exclusively or predominantly with BF, respectively. The nutritional and PMD trajectories were stable and within the normal range; there were no infants in the obesity range. In the multivariate analysis, the Communication domain was significantly associated with BMI ($p = 0.049$) and BF ($p = 0.032$). Problem Solving domain was associated with BMI ($p = 0.040$). No

Keywords:
Child Development;
Body Mass Index;
Breast Feeding;
Nutritional Status

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Edited by:
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How to cite this article: Andes pediatr. 2022;93(4):535-542. DOI: 10.32641/andespediatr.v93i4.4107

significant associations were found in the trajectories of motor and socio-individual domains. **Conclusion:** The nutritional trajectories and each PMD domains were stable and within normal ranges. Exclusive BF was associated with a better Communication trajectory, while the BMI was associated with better Communication and Problem-Solving.

Introduction

Breastfeeding (BF) is the ideal feeding for children. For this reason, international organizations promote it as a protective factor in the whole process of development and growth of human beings[1]. The World Health Organization (WHO) recommends exclusive breastfeeding (EBF) until the sixth month of life because it is one of the most cost-effective ways to ensure the health and survival of children[2]. Children breastfed for longer periods have better immunity development, lower morbidity, better cognitive function, and adequate motor development in childhood and adolescence, which would lead to a better physical condition and lower rates of obesity compared with non-breastfed children[3-8].

A longer duration of BF is associated with optimal psychomotor development (PMD)[9]. It has been shown that the proportion of children who achieved specific psychomotor milestones increased consistently with a longer duration of BF, with a lower risk of developmental delay in children breastfed for more than 6 months[5]. However, other authors point out that the observable benefits of prolonged BF would be obtained only if it is associated with positive parenting behaviors[10].

Regarding the relationship between PMD and nutritional status, an inverse association between motor development and obesity has been described[11]. In this regard, overweight infants are about twice as likely to have lower psychomotor test scores compared with eutrophic infants, and so would infants with higher subcutaneous fat[12]. Other studies suggest that in healthy populations, the achievement of motor milestones is independent of variations in physical growth[13].

Studies that have investigated typical developmental trajectories in childhood in different developmental areas present various results[14-16]. Such variety could be due to the specific assessment of certain areas, particular characteristics of the sample, and the use of different instruments and methodologies. Knowing the relationship between developmental trajectories with nutritional status and BF intake in healthy children could provide relevant information for the surveillance of children's growth and development and establish specific reference curves for each area or domain like those nutritional curves by the WHO[17].

The objective of this study was to describe and evaluate possible associations between PMD trajectories, considering the dimensions of Communication, Gross Motor, Fine Motor, Problem-Solving, and Socio-individual, and nutritional trajectories in infants fed with predominant or exclusive BF.

Subjects and Method

Prospective cohort study of infants born in 2013, from the commune of Macul, in the Metropolitan Region, Chile. The sample was obtained from the population seen at the primary level of the public health system of the country.

Consecutive sampling was performed among those infants who attended with their mothers the well-child visits, between 2013 and 2016. The participation of the infants and their mothers took place after a process of informed consent.

Term infants, without known pathology, fed with predominant or exclusive BF participated. Infants who were not predominantly breastfed, with unreliable BF intake measurement, and those who did not comply with at least 2 PMD evaluations during the follow-up period were excluded, as well as those unreliable assessments that were not correctly filled in the PMD questionnaires (figure 1).

The children were admitted at 3 months of age when BF intake was measured using the dose-to-mother deuterium technique and a bio-socio-demographic form was completed. Subsequently, the infants were seen at 4, 6, 8, 12, 18, and 30 months of age for PMD evaluation using the Ages and Stages Questionnaire (ASQ-3)[18], and weight and length were recorded to calculate the body mass index (BMI).

Measurements and Instruments

Measurement of BF intake by deuterium isotope technique: this technique allows objective measurement of the BF volume and other liquids ingested by the infant, based on a two-compartment model, by measuring the deuterium concentration in the saliva of mother and child[19]. Since deuterium is innocuous and its use in humans has not documented adverse effects, the use of this methodology is considered the most

appropriate, objective, and accurate for evaluating the pediatric population[20].

On the first day of the study (day 0), the mother and child were weighed, and basal saliva samples were collected. Subsequently, the mother ingested 30g of deuterium oxide and then breastfed her child normally. Afterward, 6 post-dose saliva samples (2 ml) were collected from the mother and the infant on established days (1, 2, 3, 4, 13, and 14) at the same times[21, 22].

Deuterium enrichment in saliva samples was measured by isotope-ratio mass spectrometry. BF intake and water intake from sources other than milk were calculated by adjusting deuterium enrichment data to models of maternal and infant body water turnover.

EBF was considered when the child ingested up to 86.6 ml/day of liquids other than BF[23] and predominant when the volume of BF intake was greater than that of other liquids ingested.

Ages and Stages Questionnaire third edition (ASQ-3)[18]: A parent-report screening questionnaire widely used for PMD assessment of children aged 2 months to 5 years. In Chile, the 8-, 18-, and 30-months questionnaires were validated[24,25]. For this study, the scores were translated into Z-scores, considering as a reference the validation scores in the United States, which are valid for Chile[26].

The ASQ-3 was given to the parents in the different visits according to the respective age range. ASQ-3 evaluates 5 developmental domains: Communication, Gross Motor, Fine Motor, Problem-Solving, and Socio-individual, with 6 questions in each domain. A maximum score of 60 can be achieved which is calculated as whether the child presents the behavior (10 points), whether she/he occasionally presented it (5 points), and whether she/he does not present it yet (0 points).

Nutritional evaluation by body mass index (BMI): The weight of the infants was evaluated with the infant naked on a SECA pediatric scale and their length was measured in the supine position using an infantometer of the same brand. For the interpretation of the anthropometric data, the BMI-for-age indicator (BMI/A) was used with the ANTHRO software. It was analyzed as a continuous variable with Z-scores[17].

Bio-socio-demographic variables: A survey was applied to the mothers at the beginning of the study, including sex, type of birth, siblings, age, years of education, and occupation.

The study was approved by the Ethics Committee of the INTA of the University of Chile.

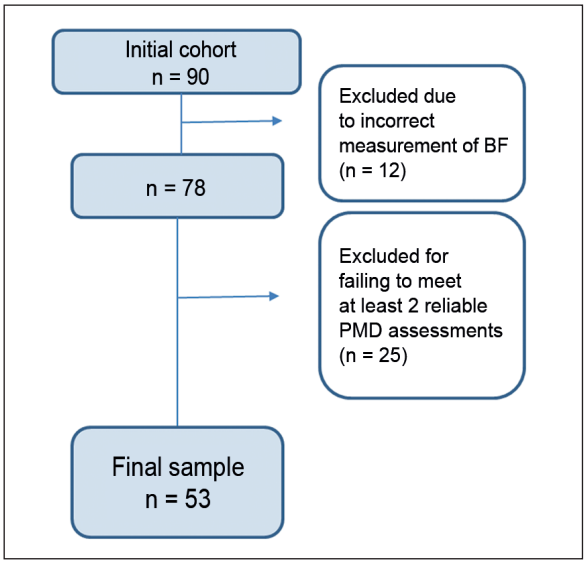

Figure 1. Flow diagram of participants. BF= Breastfeeding; PMD= Psychomotor Development.

Statistical analysis

Exploratory study including the entire recruited sample. An exploratory descriptive analysis was performed for all the variables included, considering summary measures for quantitative variables and frequency distributions for qualitative ones.

For the analysis of trajectories, scores were translated into Z-scores. For BMI, reference values from the nutritional BMI curves through the ANTHRO software were used[17], while for developmental scores, the scores from the ASQ-3 validation in the original study were considered as references[18]. PMD and BMI were analyzed using trajectory graphs considering the Z-score obtained at 4, 6, 8, 12, 18, and 30 months.

PMD, BMI, and BF trajectories were controlled for bio-socio-demographic factors in a multivariate model. Breastfeeding was analyzed as a categorical variable (exclusive versus predominant BF), while BMI was analyzed as a continuous variable. Differences between developmental trajectories and BMI were analyzed by one-way ANOVA and Bonferroni test.

Statistical difference was considered with $p < 0.05$. STATA 15.0 software was used.

Results

Ninety infants and their mothers participated. We excluded n = 12 due to error in the measurement results of BF intake and n = 25 due to not complying with at least 2 reliable developmental assessments, resulting in a sample of 53 infants (figure 1). When comparing the general characteristics of the included and exclu-

ded infants, it was observed that they showed similar characteristics in distribution according to sex, weight, length, and BMI (table 1).

Of the total infants included, 60% were male. Most of the infants were born by vaginal delivery (64%). At the age of 3 months (study entry), all infants were predominantly receiving BF and of these, 62% were fed with EBF and 76% were eutrophic. No child remained in the obese range throughout the study.

Regarding the characteristics of the mothers, 28% were younger than 20 years of age and 62% had 14 years of education (table 2). The mean BF intake of the study sample was 850.16 ± 218.7 ml and 125.84 ± 218.5 ml of other liquids.

In the analysis of PMD and BMI trajectories, there were statistically significant differences between the means of the developmental assessments in the Communication domain between months 4 and 6 (p = .035), 6 and 30 (p = 0.020), and 8 and 30 (p = 0.036), and in the Problem-Solving domain in month 4 and 6 (p = 0.043). Despite these differences, developmental trajectories in all areas, as well as BMI, remained stable and within the normal range throughout follow-up (figure 2 a, b, c, d, e, and f).

The multivariate analysis of the trajectories of each area of development according to BMI and BF (exclusive or predominant) by sex, number of siblings, type of delivery/birth, age, and educational level of the mother, showed that in the Communication domain, the BMI variable was statistically significant (p = 0.049; coef = 0.65), which showed that children with a normal BMI trajectory, but with higher values, presented, on average, a higher level of development of communication skills. Regarding the BF variable (p = 0.032 coef = -0.82), children with non-exclusive BF showed on average a lower development in this type of skills than children with EBF.

Regarding the Problem-Solving domain, the variable BMI was significant (p = 0.040 coef = 0.98), observing that children with normal BMI trajectory with high values, presented a higher level of development in this domain. It is important to highlight that children with predominant BF and EBF presented developmental trajectories within normal ranges, the same occurring with BMI.

In the trajectories of the Fine Motor, Gross Motor, Socio-individual, and BMI domains, no significant differences were found according to the analysis of the variables studied (table 3).

Table 1. Subjects included and excluded at the beginning of the study at 3 months of life*

	Included n = 53	Excluded **n = 37	p value
Female sex	39.6%	39.4%	NS
weight (kg) at admission (M/SD)	6.46 ± 0.67	6.45 ± 0.72	NS
length (cm) at admission (M/SD)	60.37 ± 2.01	60.05 ± 2.29	NS
Z score BMI at admission (M/SD)	0.54 ± 0.89	0.81 ± 0.84	NS
Mother's age	27.13 ± 6.37	29.5 ± 6.31	NS

*n = 37 excluded (12 for incorrect measurement of milk intake and 25 for not presenting at least 2 developmental assessment at the beginning and at one year of follow-up). M: Mean; SD: Standard Deviation; BMI: Body Mass Index.

Table 2. Bio-socio-demographic variables of the study sample

	n	%
Infant data		
Female	21	39.6
Vaginal delivery	34	64.15
Eutrophic at study entry	40	75.5
Exclusive breastfeeding	33	62.26
No siblings	33	62.26
Mother's data		
Age < 20 years	15	28.30
Education < 14 years	33	62.26
Occupation: housewife	48	90.57

Discussion

In our sample of infants fed with exclusive or predominant BF at the age of 3 months, the trajectories of PMD and BMI were stable and within normal ranges during the entire follow-up period of the study. It was suggested that biological factors such as nutritional status and BF could determine different developmental trajectories, which could be demonstrated for some domains related to cognitive development, such as Communication and Problem-Solving, but not for motor areas.

The Communication and Problem-Solving domains presented greater heterogeneity, with statistical differences between the means of some assessments. Valla et al. described that most infants' developmental trajectories measured with ASQs were generally positive and stable at follow-up from 4 to 24 months of age. However, for Communication and Gross Motor skills, there was more heterogeneity[14]. In contrast, studies indicate that there is significant variability in the developmental patterns of children, especially in the Fine/Gross Motor and Communication areas, which could be associated with family, sociodemographic,

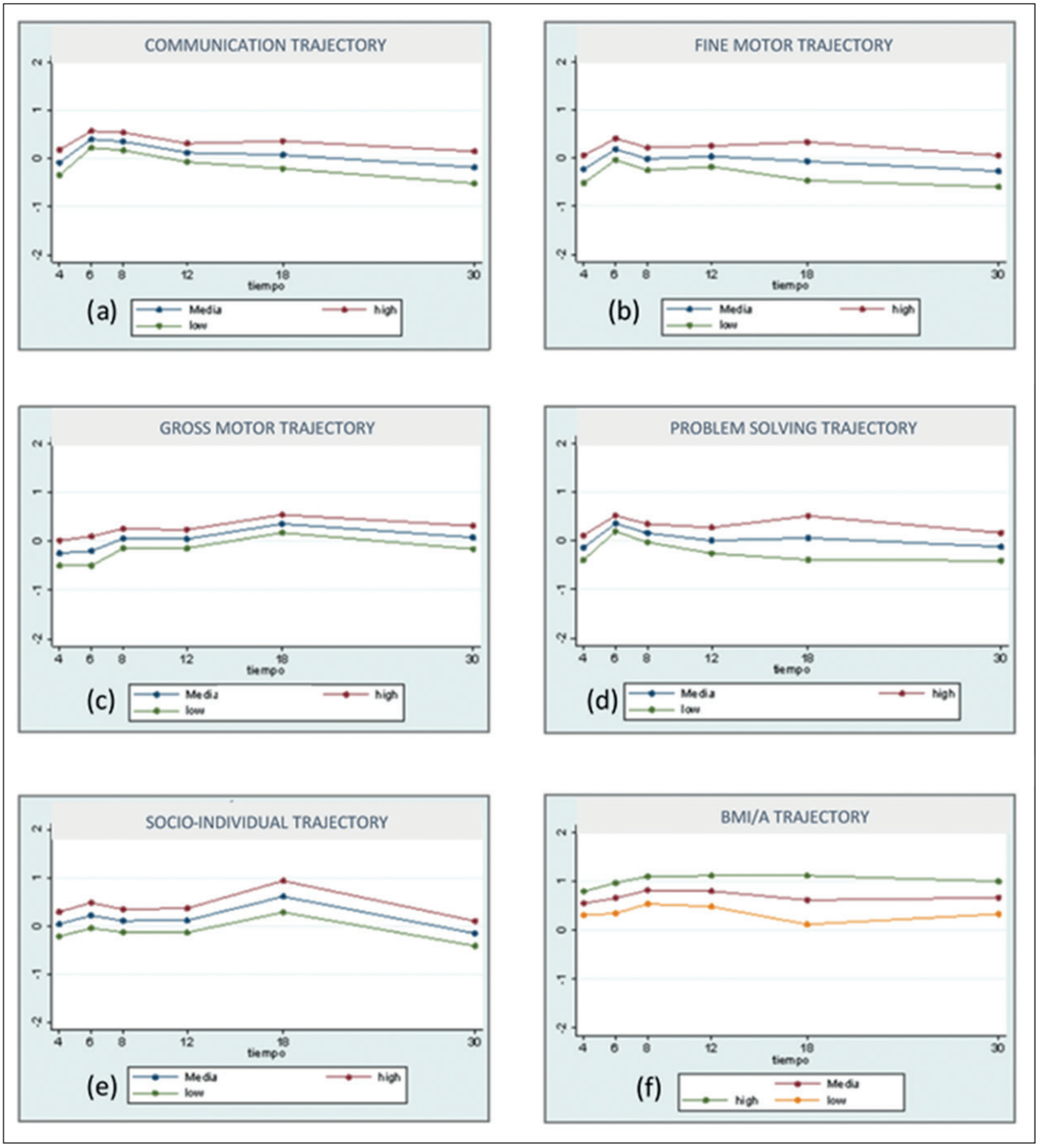

Figure 2. Development trajectories in all areas **(a)** Communication **(b)** Fine Motor **(c)** Gross Motor, **(d)** Problem Solving **(e)** Socio-Individual and **(f)** body mass index for age (BMI/A).

and socioeconomic variables, in addition to biological variables such as prematurity[14,27,28].

The BMI trajectory with high values within the normal range was associated with higher developmental scores in the domains of Communication and Problem-Solving, without finding a relationship with the areas of Fine and Gross Motor skills. In relation to this, the literature has reported differing results. Nervik et al. proposed an inverse relationship between BMI and gross motor development in children between 3 and 5 years of age[29]. In a cross-sectional investigation with 28 children aged 6 to 24 months, Camargos et al. showed a significant inverse association between BMI and level of development in motor and cognitive areas[11]. In the same line, a study by Amouian et al. showed in 90 preschool children, a lower development in the obese and

Table 3. Analysis of factors associated with development trajectories. Multivariate model for body mass index for age (BMI/A) and breastfeeding

	Communication	Fine Motor	Gross Motor	Socio-individual	Problem Solving
Greatest trajectory of BMI	0.65 (0.001 a 1.31)*	NS	NS	NS	0.98 (0.04 a 1.92)*
Non-exclusive breastfeeding (compared to exclusive)	-0.82 (-1.5 a -0. 06)*	NS	NS	NS	NS

Coefficient and Confidence Intervals 95%. Control variables: sex, number of brothers, type of childbirth, mother's data (age, years of education). *p < 0.05. BMI: Body mass index.

overweight group compared with eutrophic children according to the Denver test and ASQ[30]. Longitudinal studies have also found lower levels of motor development in obese infants compared with eutrophic ones, as Slining et al. report in 217 infants aged from 3 to 18 months[12]. These differences could be explained, in part, by the different designs and instruments used, as well as the characteristics of the sample, such as age, biological/social reality, and probably the protective effect of high BF intake[9,11,12,30].

When comparing by type of breastfeeding, it was observed that children who received EBF at 3 months presented a higher level of communication development than children who were predominantly breastfed. The results are consistent with the strong evidence that exists on the link between BF and future cognitive development such as, for example, better memory retention and greater language skills, and would also be associated with better results in general development[5,31,32].

In a cohort of 13,000 mother-child pairs, Kramer et al. reported that those children who maintained prolonged EBF obtained higher intelligence scores at 6 and 16 years of age[33,34]. Studies analyzing EBF during the first year of life describe a positive association with early language development and motor skills at 4 and 14 months[35,36].

Among the limitations of the study is its exploratory nature, with a small and homogeneous sample in terms of high breastfeeding intake and nutritional status, therefore, it is likely that other significant associations were not found. There was a 41% loss in the initial cohort, although no significant differences were demonstrated between infants included and those excluded from the study (table 1). On the other hand, BF was measured only at 3 months and its continuity over the following 2 years is unknown.

The strengths of the study include its longitudinal design and the use of the method considered the reference standard for measuring BF intake[37], as well as the use of the ASQ-3 which is an internationally validated screening method that has proven to be reliable for the evaluation and monitoring of development in children[24,38]. In addition, due to its low cost and accessibility, it can be applied in successive evaluations and allows for comparing the results with international experiences[9,14,39,40].

We can conclude that in children fed exclusively or predominantly with BF, the trajectories of BMI and developmental domains were stable and within normal ranges throughout the follow-up. Even so, in the Communication domain, children with EBF presented a higher level of development than children with predominant BF. A BMI trajectory with high values within normality was associated with higher developmental levels in the Communication and Problem-Solving domains, with no differences found in the motor areas.

It seems important to extend this analysis to longer-term longitudinal studies. Knowing the normative pattern of children's developmental trajectories is very relevant for the establishment of public policies that promote child health surveillance.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

The study was financed with funds granted by the International Atomic Energy Agency (IAEA) of the United Nations and with our own funds

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