OPEN ACCESS Freely available online

Journal of Nutrition & Food Sciences

ISSN: 2155-9600

Research Article

Nutritional Assessment in Children with Allergy to Cow's Milk Protein

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ABSTRACT

Objective: To relate the nutritional status of children allergic to cow's milk protein to the factors that interfere in the nutritional deficit.

Methodology: It is a descriptive cross-sectional and quantitative approach carried out in the outpatient clinic for food allergy of a Children's Hospital in Ceara, whose sampling is non-probabilistic sample of convenience and includes children up to 48 months of age. The variables of interest were: sex, age, age at diagnosis, duration of exclusive breastfeeding, use of infant formula, weight and stature. The data collection was carried out from March to June 2015 through anthropometric measurements (weight and height) and the application of a semi-structured questionnaire. The statistical analysis related and associated all the variables, obtaining as a result significant $p<0.05$.

Results: The study included 342 children with a mean age of 7.50 months (± 6.51), being 53.50% boys and 46.50% girls. The average weight of the population was 8.03 kg (± 3.85), height was 67.68 cm (± 9.66) and BMI was 17.22 Kg/m^2 (± 8.87). The average time for diagnosis of allergy to cow's milk protein was 8.98 months (± 7.90) and the average time of exclusive breastfeeding was 2.58 months (± 2.16).

Conclusions: It was found that there was adequacy of weight and height in most children. However, some factors may have positively influenced the results as: age at which the allergy was diagnosed, age at which there was introduction of formulas, duration of breastfeeding and participation in the program of cow's milk protein allergy.

Keywords: Breastfeeding; Food hypersensitivity; Child

INTRODUCTION

Food allergy (FA) is a specific immune response manifested to exposure to a particular food, when the reaction is clinically abnormal to cow's milk protein β-lactalbumin and β-lactoglobulin and casein leading to an inflammatory process and affecting mainly the skin and the gastrointestinal tract, it can be said that this allergy is a cow's milk protein (ACMP) [1-3].

In the pediatric age, the global prevalence of food allergy has increased over the last 30 years in 6 to 8% and the ACMP varies between 4 to 6% [4,5]. The estimate is a prevalence that varies between 1 to 8% in children and 1 to 2% in the adult population of the European continent and a prevalence of 5% in children younger than 3 years and 4% in North American adults [6].

Some factors can be considered at risk for the development of ACMP, such as, for example, genetics, gender, early weaning, time of introduction of cow milk (CM), ethnicity, changes in diet (vitamin D, type of fat, antioxidants, obesity), the hygiene hypothesis (reduction of exposure to infectious agents, parasites, type of intestinal colonization) and exposure to food allergens (pregnancy, breast, milk weaning, through the skin) [7].

Breast milk (BM), as the first food that the child comes in contact, is a vector to be considered in the development of ACMP, because it has not been executed correctly the maternal milk exclusion

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Received: March 31, 2021; **Accepted:** April 14, 2021; **Published:** April 21, 2021

Citation: Nunes MPO, Lustosa AMP, Ribeiro HB, Filho JCCN, Guedes MIF (2021) Nutritional Assessment in Children with Allergy to Cow's Milk Protein. J Nutr Food Sci. 11:801.

diet, however it is the main method of avoiding the development of allergies [3,8].

In nursing infants fed with formula, the most suitable type as a first diet is an extensively hydrolyzed (eHF) formula with proven efficacy in ACMP [9,10]. If no improvement is observed within 2-4 weeks, the cause of the allergic reaction may be the peptides remaining in the eHF, particularly if the infant is exposed to multiple foods. In such patients, it is recommended to try the formula of aminoacids (AAF) before the symptoms disappear. Furthermore, in the case of extremely severe symptoms or life-threatening conditions, the first choice must be the AAF [9].

When the food introduction is not done correctly, or the diagnosis is time consuming and not accurate, symptoms such as anorexia, melena, intestinal malabsorption and loss of nutrients in the episodes of regurgitation, diarrhea and vomiting can be manifested in children diagnosed with ACMP, leading to nutritional changes such as growth deficiency and malnutrition protein-calorie intake due to the immaturity of the barrier of the intestinal mucosa present in the first months of life [3,11,12].

In order to classify the nutritional status during childhood it is necessary to carry out an anthropometric assessment based on the measurement of weight and height, and calculate the body mass index (BMI) resulting in the diagnosis through the growth curves recommended by the World Health Organization in 2006 [13].

Given the above, the introduction of food and the quick and reliable diagnosis of cow's milk protein allergy in children allow greater probability of adequacy of weight and height for age, besides making it possible to reverse the nutritional framework, when there is a risk of anthropometric deficits caused by allergic manifestations.

Thus, the objective of this study was to relate the nutritional status of children allergic to CMP to the factors that impact the nutritional deficit.

METHODOLOGY

This is a descriptive cross-sectional and quantitative approach which is part of a larger survey entitled "Development of techniques for the diagnosis of food allergy". This study was performed at the outpatient clinic of food allergies in a children's hospital located in Fortaleza/CE.

The children care program for infants allergic to cow's milk protein is funded by the State Government of Ceará through which more than 1000 allergic children receive multiprofessional monitoring and infant formulas when necessary.

The sample in this study is non-probabilistic sample of convenience and includes children up to 48 months of age treated in the outpatient clinic. Included are all the children whose guardians agreed to participate in the study by signing the informed consent form, and excluded the children who were hospitalized or who were making use of immunosuppressant drugs.

The variables of interest were: sex, age during the data collection period, age at diagnosis, duration of exclusive breastfeeding (EBF), age of introduction of infant formula, type of formula, children, weight, height, BMI to assess possible déficit in weight and height gain.

The data collection was carried out from Fevereiro to Setembro 2015 through anthropometric measurements (weight and height), implementation of the protocol of care for ambulatory care during a medical consultation and a semi-structured questionnaire with open and closed questions to supplement the information.

For the nutritional assessment, the anthropometric values were assessed by Z-score pursuant to the children classification of the World Health Organization (2006), for the children who presented an appropriate weight index for age when (>Z-Score-2 and <Z-Score+2), being considered values below -2 children with low weight at birth or very low weight for age, and above +2 children with heavy weight for age.

For the height index for age, it was considered adequate when the value was greater than -2, and the values below this value were deemed short stature or very low height for age. Another assessment, the weight vs. height, considered adequate when the results were between >-2 and <+1, the measurements below -2 were considered underweight or accentuated thinness, and above +1 as being overweight or obese. For the BMI index for age it was considered appropriate when the results were between >-2 and <+1, the measurements below -2 was considered underweight or accentuated thinness, and above +1 as being overweight or obese. All the anthropometric diagnostics were evaluated by the program ANTHRO® (version 3.2.2, January 2011).

The statistical analyses in this study were performed in R software, version 3.2.2. The data were expressed as frequencies, percentages, minimum and maximum values, measures of central tendency and dispersion. We tested the normality of the data using the Kolmogorov-Smirnov test and the homogeneity of the data using the Levene test. For the comparison between two means, with normal data and homogeneous, we used the Student's t-test for independent samples. For the comparison between three or more means, when the data were normal and homogeneous, we used the ANOVA test, and when not, we used the Kruskal-Wallis test. We tested the association between category variables using the Chi-square test, which showed values higher than 5, and chi-square test of Fisher, which presented values lower than 5, being considered significant only when p values were below 0.05.

The study complies with resolution No. 466 of 12 December 2012, which approved the guidelines and regulatory standards

for research involving humans. This project is part of the research approved by the ethics committee of Universidade Estadual do Ceará (no 2-26108713.6.0000.5534).

RESULTS

342 children aged between 15 days and 48 months and average of 7.50 months (± 6.51) met the inclusion and exclusion criteria, being 53.50% (183) boys and 46.50% (159) girls. The average weight of the population was 8.03 kg (± 3.85), height was 67.68 cm (± 9.66) and BMI was 17.22 Kg/m2 (± 8.87). The average time of diagnosis of allergy to cow's milk protein was 8.98 months (± 7.90) and the average time of exclusive breastfeeding was 2.58 months (± 2.16).

As for the duration of exclusive breastfeeding and adequacy of nutritional status, there was no significant difference in the classification of height and age (H/A), weight and age (W/A), weight and height (W/H) and body mass index (BMI/I) in the 342 children who received BM on average 2.58 months (± 2.16) (p>0.05) (Table 1).

Table 1: Comparison of mean duration of breastfeeding between classifications of anthropometric status.

Variable	Classification	Duration of exclusive breastfeeding (months)				P
		N	A minimum	Most	Mean (SD)	
E/I	Appropriate	252	0	7	2.71 (2.15)	0.117£
	Low Height	34	0	7	2.45 (2.22)	
	Very low height	56	0	6	2.06 (2.09)	
P/I	Appropriate weight for age	232	0	7	2.71 (2.14)	0.223£
	Low weight for age	43	0	6	2.21 (2.01)	
	Heavy weight for age	67	0	6	2.34 (2.27)	
P/E	Appropriate weight for height	246	0	7	2.63 (2.14)	0.257‡
	Low weight for height	36	0	6	1.95 (1.86)	
	Heavy weight for height	60	0	6	2.74 (2.36)	
Bmi/I	Appropriate BMI for age	230	0	7	2.64 (2.13)	0.326£
	Low BMI for age	36	0	6	1.95 (1.86)	
	Overweight	31	0	6	2.72 (2.25)	
	Obesity	45	0	6	2.66 (2.43)	

Note: I-age; E-height; P-weight; BMI-Body mass index; £-ANOVA test; ‡-the Kruskal-Wallis test. Different letters indicate significant differences between the means. P value considered significant below 5%.

The nutritional status was also related to age at diagnosis or initial consultation on the program of allergy to cow's milk protein, which has been considered early under 6 months of age and late above that number, so there was no statistically significant association between the classification of age at diagnosis and the classification of, W/A and BMI/I (p>0.05) as shown in Table 1.

When related the use of infant formula with the classification of anthropometric status, there was no statistically significant difference between classifications of E/I, P/I and P/E (p>0.05). On the other hand, there was no statistically significant difference between the classification of the use of formulas and the classification of BMI/I. It was observed that the majority of overweight individuals, with appropriate BMI for age and low BMI for age used the FA and the majority of individuals with obesity used the FEH (p=0.023) as shown in Table 2.

Table 2: Distribution of individuals in accordance with the classifications of the use of formulas and nutritional status.

Variable	Classification	Formula										P*
		FEH		FA		LM		LV without lactose		Total		
		N	%	N	%	N	%	N	%	N	%	
E/I	Appropriate	105	41.67	143	56.75	3	1.19	1	0.4	252	73.68	0.677
	Low Stature	17	50	16	47.06	1	2.94	0	0	34	9.94	
	Very low stature	24	42.86	32	57.14	0	0	0	0	56	16.37	
	Total	146	42.69	191	55.85	4	1.17	1	0.29	342	100	
P/I	Appropriate weight for age	98	42.24	131	56.47	3	1.29	0	0	232	67.84	0.165
	Low weight for age	14	32.56	29	67.44	0	0	0	0	43	12.57	
	Heavy weight for age	34	50.75	31	46.27	1	1.49	1	1.49	67	19.59	
	Total	146	42.69	191	55.85	4	1.17	1	0.29	342	100	
P/E	Appropriate weight for height	103	41.87	141	57.32	2	0.81	0	0	246	71.93	0.05
	Low weight for height	11	30.56	24	66.67	1	2.78	0	0	36	10.53	
	Heavy weight for height	32	53.33	26	43.33	1	1.67	1	1.67	60	17.54	
	Price	146	42.69	191	55.85	4	1.17	1	0.29	342	100	
Bmi/I	Appropriate BMI for age	97	42.17	131	56.96	2	0.87	0	0	230	67.25	0.023
	Low BMI for age	11	30.56	24	66.67	1	2.78	0	0	36	10.53	
	Overweight	11	35.48	20	64.52	0	0	0	0	31	9.06	
	Obesity	27	60	16	35.56	1	2.22	1	2.22	45	13.16	
	Total	146	42.69	191	55.85	4	1.17	1	0.29	342	100	

Note: Legend: I-age; E-height; P-weight; BMI-Body mass index (BMI); *-Chi-square Test Fishers exact test. P value considered signifi cant below 5%.

When parameters were related: age, weight and height in the diagnosis, it may be observed that there is a statistically significant association between the classification of age at diagnosis and the classification of the P/E, showing that the majority of adequate weight for height and low weight for height were age at diagnosis below six months, in contrast to a greater proportion of individuals with heavy weight for height were aged over six months at diagnosis (p=0.025) (Table 3).

Table 3: Distribution of individuals in accordance with the classifications of age at diagnosis and nutritional status.

Variable	Classification	Age at diagnosis						P*
		<6 months		¥ 6 months		Price		
		N	%	N	%	N	%	
E/I	Appropriate	121	48.02	131	51.98	252	73.68	0.573
	Low Height	19	55.88	15	44.12	34	9.94	
	Very low height	25	44.64	31	55.36	56	16.37	
	Total	165	48.25	177	51.75	342	100	
P/I	Appropriate weight for age	114	49.14	118	50.86	232	67.84	0.26
	Low weight for age	24	55.81	19	44.19	43	12.57	
	Heavy weight for age	27	40.3	40	59.7	67	19.59	

	Total	165	48.25	177	51.75	342	100	
P/E	Appropriate weight for height	124	50.41	122	49.59	246	71.93	0.025
	Low weight for height	21	58.33	15	41.67	36	10.53	
	Heavy weight for height	20	33.33	40	66.67	60	17.54	
	Total	165	48.25	177	51.75	342	100	
Bmi/I	Appropriate BMI for age	115	50	115	50	230	67.25	0.163
	Low BMI for age	21	58.33	15	41.67	36	10.53	
	Overweight	13	41.94	18	58.06	31	9.06	
	Obesity	16	35.56	29	64.44	45	13.16	
	Total	165	48.25	177	51.75	342	100	

Note: Legend: *-Chi-Quadrado accurate correlation. P value considered significant below 5%.

There was no significant difference in mean weight, height and BMI, age, age at diagnosis and duration of exclusive breastfeeding when comparing the children sex (p>0.05) (Table 4). Furthermore, there was not a statistically significant association between age at diagnosis or first appointment with the ACMP program, sex and the classifications of the nutritional status of H/A, W/A, W/H, BMI/I with the formula of amino acids (FA), extensively hydrolyzed (FEH), BM and lactose-free cow milk (p>0.05).

Table 3: Distribution of individuals in accordance with the classifications of age at diagnosis and nutritional status.

Variable	Sex	N	A minimum	Most	Average	DP	P£
Weight (Kg)	Male	183	2.9	61	8.31	4.77	0.15
	Female	159	1.95	14.6	7.71	2.35	
Height (m)	Male	183	48	110	67.62	10.01	0.913
	Female	159	43	92	67.74	9.28	
BMI (Kg/m^2)	Male	183	11.72	175.24	17.89	11.92	0.135
	Female	159	10.07	27.33	16.45	2.2	
Age (months)	Male	183	0.5	67	7.38	6.78	0.732
	Female	159	1	48	7.63	6.21	
Age at diagnosis (months)	Male	183	1	67	9.06	8.41	0.853
	Female	159	1	48	8.9	7.29	
Duration of exclusive breastfeeding (months)	Male	183	0	7	2.46	2.13	0.291
	Female	159	0	7	2.71	2.18	

Note: BMI-Body mass index; SD-standard deviation; £-Student's t-test independent. P value considered significant below 5.

DISCUSSION

In this study, there was a predominance of males (183) corroborating with a study that examined a sample of 178 allergic children of which 53% were boys and another study has confirmed that likelihood, stating that there is a greater risk of atopy in males [14,15]. However, a cross-sectional study found that FA mostly affects girls up to 5,9 (± 0.7) years of age [16].

In the face of the nutritional status of children in the present study, the majority showed suitability as to height/age, weight/age, weight/height and BMI/age, thus corroborating with the study of Diaz et al., who evaluated infants under 6 months of age, pursuant to criteria of Gomez, yielding as a result, 70% eutrophic and 30% with malnutrition grade I [17].

However, the majority of studies in the literature, show a deficiency in weight and height gain, as shown by Vieira et al., who presented a 15.1% of the sample children with low weight for age (Score-Z below -2 standard deviations), 8.7% low weight for height (Score- Z less than -2 standard deviations) and 23.9% low height for age (Z-score below -2 standard deviations) [18].

A better nutritional status was observed in our study, which may be explained by the multiprofessional monitoring received by allergic children through the ACMP government program. This can be considered one of those responsible for the fact that if time of diagnosis is fast, so is the reduction of symptoms caused by allergies that lead to weight loss and decreased absorption of nutrients. Moreover, the age of arrival in the program is also

taken into consideration, since more than half had less than 3 months of age.

Pereira and Silva, explain the deficit of weight and stature gain of children with food allergies due to insufficient intake of macro and micronutrients, especially calcium, phosphorus, Vitamin D and protein, besides the losses of nutrients through gastrointestinal symptoms (diarrhea, regurgitation and vomiting), which directly influences the nutritional status [19].

Thus, in addition to the protein deficit-caloric intake, the diet that exclude cow's milk and its derivatives may also entail, deficiencies of dietary micronutrients, if there is no proper replacement of these foods that meet the recommendations, according to sex and age [20].

In this study, in which the time of EBF in children with ACMP was compared to the classifications of anthropometric indices, it was found that in children with low birth weight and very low weight for age, the average time of EBF was shorter when compared with the other classifications (Table 1). The children who had low stature and very low height for age, also showed average time of EBF less than the children with adequate height for age. These results show that the duration of breastfeeding is important for the weight and height gains.

Some meta-analyses indicate that breastfeeding, in opposition to infant formula, can directly impact on appetite and weight gain of infants through the action of bioactive components in human milk (hormones) [21].

Luccioli and colleagues concluded in their study that EBF of ≥ 4 months may have a preventive effect on the development of allergies in general after 1 year of age in children of non-high risk, and Liao et al, found the same for allergy to cow's milk protein during early childhood, because, besides helping in the growth and development, breast milk has components that are beneficial to the child allergic reaction, as shown in a research by Sato et al, which investigated whether the enrichment of diet with carotenoids inhibits oral sensitization to an antigen and the development of FA and concluded that food carotenoids supplied by BM during the early childhood may prevent the development of food allergies [22-24].

In an experimental research it was found that children exclusively fed at the breast in the first 6 months of life presented adequate weight and height gain as compared to the existing standards, having a sharp increase in first 4 months, and slowing down afterwards [25].

Some factors, such as duration of breastfeeding have been associated to the speed in weight and stature gain during the first six months of life and found a relation between the practice or predominance of EBF in the first four to six months of life and greater weight gain for the children evaluated, as compared with the intake of other milks [26].

For nursing infants not being breastfed, the milk or infant formula containing cow's milk protein or other proteins not modified of animal origin and the like should be prohibited during the diagnosis period. If the first feeding with formula based on CM or food supplement in a breastfed child causes symptoms, the formula must be changed and the elimination must be made in the child, and not in the mother's diet [1].

Therefore, the nutritional disorders in children with ACMP must be identified so that the monitoring of its treatment can be performed in a targeted and effective manner.

Growth and development deficits found in children of this study may be justified by the fact that many times they come to the first consultation of the program using inadequate infant formulas, which result in the appearance of symptoms that lead to loss of nutrients, and low weight and height gain. Some reports diverge from Yu et al., who found positive effects observed in weight and height of children with ACMP who used specific infant formulas, as compared to a healthy population [27].

A study examined 100 children aged 1 to 17 months who suffered from atopic dermatitis resulting from ACMP and found a lower average of weight and height in children who received a diet free of cow milk [28].

The effects of consuming a diet both free of cow milk and with cow milk were studied in children 2 years of age, and the results showed a significant difference in the food intake of the two groups evaluated. It was identified lower energy consumption, fat, protein, calcium, riboflavin and niacin in the group of children on a diet free of cow's milk. In the group that used CM substitutes, some improvements were observed in the diet adequacy, although it did not meet the recommendations for riboflavin and calcium [29].

In this study, when compared the use of infant formula with the classification of anthropometric status, the largest proportion of individuals with appropriate BMI for age, low BMI for age and overweight used the FA formula and the largest proportion of individuals with obesity used the FEH formula ($p=0.023$).

The Espghan and the American Academy of Pediatrics (AAP) consider the use of extensively hydrolyzed formula and aminoacids for dietary treatment of children with ACMP as first option, and the partially hydrolyzed formulas are not indicated as well as other mammal protein and milk from other mammals. Although the formulas based on soybeans are associated with a lower allergenicity than the formula based on cow's milk the concerns with the content of isoflavones (phytestrogens) were increased so that they are recommended only after 6 months of life [9].

Thus, it is important to stress that the inadequate supply of calcium can cause diseases such as rickets, osteoporosis, hypertension, cervix cancer, polycystic ovary syndrome, ovarian cancer, premenstrual syndrome, insulin resistance and obesity, which

makes a periodic monitoring of these patients it indispensable, through the continuous assessment of clinical status, nutritional and dietary intake of children during the period of exclusion of cow's milk protein in the diet [30].

Thus, the treatment for ACMP needs to be appropriate and meet the nutritional needs of children allowing its full growth and development. Otherwise, nutritional changes can lead to energy protein malnutrition, as well as in growth deficits being necessary to assess the nutritional status to find and correct the nutritional deficits, thus avoiding negative consequences of ACMP in children [11].

CONCLUSION

It was found that there was adequacy of weight and height in the majority of children, according to the parameters evaluated, which modifies the pattern found in most studies. However, some factors may have positively influenced the results, such as: age at which the allergy was diagnosed, age at which there was introduction of formula, duration of breastfeeding and participation in the ACMP program. In addition, we suggest more studies that seek to assess micronutrient deficiency in children ACMP as well as studies that relate the duration of exclusive breastfeeding proportional to the improvement of symptoms and age of oral tolerance.

FUNDING

Laboratory of Biotechnology and Molecular Biology of the State University of Ceara.

CONFLICTS OF INTEREST

Nothing to declare.

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