

Caries in children with lactose intolerance and cow's milk protein allergy

Suzely Adas Saliba MOIMAZ^(a)
Marcelo Augusto AMARAL^(a)
Cléa Adas Saliba GARBIN^(a)
Tânia Adas SALIBA^(a)
Orlando SALIBA^(a)

^(a)Universidade Estadual Paulista – Unesp,
School of Dentistry, Department of Pediatric
and Social Dentistry, Araçatuba, SP, Brazil.

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Corresponding Author:
Suzely Adas Saliba Moimaz
E-mail: sasaliba@foa.unesp.br

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Abstract: Dental caries in 5-to-8-year-old children with cow's milk protein allergy (CMPA) and lactose intolerance (LI), their treatment needs, and the consumption of milk-based products and milk derivatives by these patients were investigated. A cross-sectional study was undertaken with 200 children in southern Brazil in 2017. The clinical examination was based on the World Health Organization criteria and a questionnaire was sent to parents or legal guardians to collect information on the children's food intake, pre-existing systemic diseases, medication use, and CMPA and LI. Standardization was performed to verify concordance among examiners ($\kappa = 0.96$). Caries prevalence was 67.50% in children with CMPA or LI, but 34.37% in those without these conditions. The mean dmft (decayed, missing, and filled teeth) index in children with CMPA or LI was 1.75 ± 1.84 , significantly higher than among non-allergic or lactose-tolerant children (0.83 ± 1.60) ($p < 0.001$). In children with CMPA or LI, the mean for treatment needs was 1.58 ± 1.50 . Lactose-free milk was the most frequently consumed food among allergic/intolerant children (65.00%), with a mean dmft of 2.00 ± 2.08 , higher than that obtained for those without CMPA/LI (0.82 ± 0.87), showing no significant difference ($p = 0.129$). Although dental caries and treatment needs in primary dentition were associated with CMPA or LI, children's intake of replacement foods did not pose any risk for the development of carious lesions. Statistically significant differences were obtained for the prevalence and severity of dental caries. This shows the need for treatment of children with CMPA or LI, who had the worst caries prevalence and severity rates.

Keywords: Dental Caries; Milk Hypersensitivity; Lactose Intolerance.

Introduction

Food allergy is a public health concern since it affects 6 to 8% of children and 2% of adults worldwide.^{1,2} Its self-reported prevalence in adults and children in European populations hovers around 5.9% and 6.9%, respectively.³ Cow's milk protein allergy (CMPA) is the most common allergy in children.^{4,5} Although rare, there have been reports in recent decades on an increase in CMPA prevalence. In fact, severe food allergy has been currently the main cause of emergency care in the hospital setting.⁶

CMPA may be defined as an adverse immunological reaction to one or more cow's milk proteins.⁷ The reaction involves immunoglobulin E (IgE), lymphocytes T, or both, affecting 2-3% of children.⁴ There is no consensus among patients and physicians about lactose intolerance (LI) and CMPA.



Several discussions on the nomenclature of allergic reactions to milk and on diagnosis have ensued in the past 15 years.⁸ The current nomenclature has been determined by the mechanisms that most probably cause the symptoms. CMPA is mediated by IgE. LI is the reduced capacity of the small intestine to digest lactose and it is not immune-mediated.^{8,9}

In Brazil, 43% of white and mixed-race adults have LI, but it is more frequent among black people and among individuals of Japanese ancestry, with typical and systemic symptoms. Typical symptoms include bellyache, bloating, flatulence, diarrhea, stomach rumble, and vomiting, especially in young people. Feces are bulky, foamy, and watery.¹⁰ In the case of systemic symptoms, it must be ascertained that they are really caused by food intolerance, or rather, whether they are coincident symptoms or derived from CMPA (affecting 20% of people with LI symptoms).¹¹

Total and/or definitive exclusion of lactose from the diet of children with CMPA or LI depends on a precise medical diagnosis and normally involves soy-based formulas or other milk substitutions, sweetened or not with sucrose and nutritionally adequate,¹² whose capacity to cause enamel demineralization of deciduous teeth and to form biofilm is poorly known.¹³

Children with special healthcare needs, such as those with fragile X syndrome¹⁵, growth disorders, gastroesophageal reflux, and IL, are prone to oral diseases.¹⁴ Dentists are, therefore, better prepared to identify children at high risk for dental caries and other oral diseases, which allows for an early intervention.¹⁶

Studies on the dental conditions of children with CMPA or LI are highly relevant because they assess caries prevalence and other oral diseases that affect this specific group. Most studies on CMPA or LI patients deal with medical and nutritional aspects.^{2,5,8,17} In fact, scanty information is available on the oral conditions of children with CMPA or LI.^{18,19} The topic is rarely investigated. The present study analyzes the prevalence and severity of dental caries and the treatment needs of 5-to-8-year-old children with CMPA or LI. Some factors related to this specific health condition are also evaluated.

Methodology

The present cross-sectional study analyzes the prevalence and severity of dental caries, treatment needs, and the intake of supplemental formulas by children attending a private school in a town in southern Brazil, in 2017.

Study population and data collection

The study population was comprised of male and female 5-to-8-year-old children. This specific age bracket was chosen since primary LI mainly manifests itself after 6 years in white individuals.²⁰ Prior to the clinical examination, a food frequency questionnaire (FFQ) was sent to parents or legal guardians for evaluation of children's consumption of milk, milk derivatives, and other foods. Whether or not the children had CMPA or LI, all parents or legal guardians answered the FFQ. In addition to the FFQ, another questionnaire including data on CMPA and its duration, LI and its duration, systemic disease, and use of medications was sent out. It should be underscored that CMPA and LI were either identified through parents' or legal guardians' responses to the questionnaires or self-reported.

The distinction between the two diseases in the questionnaire was based on the description of the main symptoms. LI is characterized only by gastrointestinal symptoms (abdominal pain, flatulence, and diarrhea), while CMPA has gastrointestinal, dermatological, and/or respiratory symptoms.⁸

The sample size was based on an error rate of 5% and on a 95% confidence interval. Prevalence of lactose malabsorption was estimated at 10.5%²¹ and the minimum sample size was set at 145 children. Since dental caries and treatment needs of the study population were evaluated, the sample size was larger in order to make up for possible losses. In fact, the number of children in the current study was 200.

A pilot study with 10 children of the same age was undertaken. These children were not chosen for the final sample, which included a health questionnaire and FFQ pretest. The intra-examiner calibration consisted of a 4-hour theoretical step on the dental indices used and of a 16-hour practical step involving tests and discussions with the first author of the present

paper.²² Tests were performed in duplicate in 10% of the sample (20 children). Kappa statistics was used to calculate reproducibility, with one tooth as the diagnostic unit, following the methodology proposed by Peres et al.²² These tests aimed at benchmarking the diagnostic reliability of the initial examination. The kappa coefficient was 0.96.

The final sample included the children who returned the FFQ, the questionnaire on health conditions, and the signed free consent form. Later, the children were subjected to an oral clinical examination. Children with severe systemic or neurological diseases, with viral diseases, who were wearing orthodontic appliances, and who did not forward all the required documents to the school authorities after three school visits were excluded from the study.

If treatment needs or immediate dental care were detected during the examination, the child was taken to a basic health unit for proper treatment.

Food frequency questionnaire for adolescents

The food frequency questionnaire for adolescents (FFQA), prepared by Slater et al.²³ to evaluate the amount of food consumed throughout 6 months, was adapted and employed in the current research. Adaptation was required since FFQA failed to include soy-based foods. FFQA was validated by Marchioni et al.²⁴ and proved to be satisfactory.

FFQA comprises 76 food items or food groups, featuring approximately 90% of the energy and macronutrients consumed by children and adolescents. The list of items was based on the data on food consumed in the last 24 hours. Each food item in the questionnaire comprised seven categories, and both the amount and frequency of food consumption were recorded. Categories, determined in quantities (standard portion) consumed during the day, were characterized as lack of intake ('never') and frequency ('twice a day or more')

The questionnaire was sent out to the parents or legal guardians, who were invited to estimate the mean frequency of food intake during the past 6 months, choosing one out of seven categories: "never," "less than once a month," "once to three times a month," "once a week," "twice to four times a week," "once a day," or "twice a day or more."

The following food types were included in the categories: whole milk, semi-skimmed milk, or skimmed milk; plain yogurt or fruit yogurt; chocolate milk; lactose-free milk; whole soy milk; soy milk powder; soy yogurt; chocolate soy milk; soy milk fruit juice; other types of milk.

The foods described above were classified as high, moderate, and low consumption. High-consumption foods are those eaten once a day or twice a day or more; moderate-consumption foods are eaten twice to four times a week; any other options indicated low-consumption foods.

Results included only those foods with a consumption greater than 15% in the moderate and low consumption categories.

Clinical examination

All of the children participated in activities related to oral health in the first clinical evaluation. They received toothbrushes and performed supervised toothbrushing. After the first contact with the children, a trained examiner performed the dental clinical examination.

All the children were examined in a room within the school premises, under good natural lighting. When necessary, illumination was provided by a portable flashlight. The examiner wore surgical mask and gloves and performed the examination in the standing position. He used probes with ball tips and previously sterilized plane mouth mirrors in compliance with biosafety standards.

The codes and criteria for classification followed the fourth edition of the Oral Health Surveys, Basic Methods²⁵ for retrieval of clinical data on dental conditions (dmft) and the index of treatment needs (ITN).

The field team consisted of an examiner (the second author) and a note taker (an undergraduate dental student) who had to write down the details of the clinical examination.

Data processing and analysis

BioEstat v. 5.3 (Instituto Mamirauá, Manaus, Brazil) and EpiInfo v. 7.1.5 (Centers for Disease Control and Prevention, Atlanta, USA) were employed for data processing. The Mann-Whitney U test was used to test dmft and ITN indices in the groups with and without CMPA or LI. The chi-square test was used to

analyze proportions (prevalence of dental caries and treatment needs) between the groups. Nonparametric tests were employed since the dmft index did not have a normal distribution. Statistical significance was set at 5%.

Ethical aspects

The study was approved by the Research Ethics Committee of the Centro Universitário de Maringá (UniCesumar), process number 2.028.098/2017, and complied with Resolution 466/2012 of the Brazilian Health Council. Parents or legal guardians received information on the aims of the study and signed the consent form for the participation of their children.

Results

Sample description

The present study on children's oral health carried out in a town in southern Brazil revealed a balanced distribution between patients' age and sex, with a slight predomination of 6-year-old children (36.50%) and males (59.00%). Six children (3.00%) had only CMPA, 37 (18.50%) had only LI, and three (1.50%) had both CMPA and LI. Forty children (20.00%) were allergic to cow's milk protein or intolerant to lactose. Intolerance duration ranged from 12 to 92 months. In addition, drug treatment of lactose malabsorption was identified in seven children (17.50%) with CMPA or LI (Table 1).

Table 1. Epidemiological and clinical characteristics of children (n=200). Paraná, Southern Brazil, 2018.

Variables	Total (n=200)	Children without CMPA + LI (n = 160)	Children with CMPA + LI (n = 40)	p-value
Age (years)	05-08	05-08	05-08	
mean ± SD	6.26 ± 0.94	6.23 ± 0.96	6.38 ± 0.81	
Median	6	6	6	0.263
Age range	n (%)	n (%)	n (%)	
5 years	48 (24.00)	42 (26.25)	06 (15.00)	
6 years	73 (36.50)	58 (36.25)	15 (37.50)	
7 years	59 (29.50)	42 (26.25)	17 (42.50)	
8 years	20 (10.00)	18 (11.25)	02 (5.00)	
Sex	n (%)	n (%)	n (%)	
Female	82 (41.00)	62 (38.75)	20 (50.00)	
Male	118 (59.00)	98 (61.25)	20 (50.00)	
CMPA	n (%)	n (%)	n (%)	
No	194 (97.00)	-	37 (92.50)	
Yes	06 (3.00)	-	03 (7.50)	
Allergy duration (months)	40-78	-	40-78	
mean ± SD	1.78 ± 10.38	-	8.90 ± 22.01	
Median	0	-	0	
LI	n (%)	n (%)	n (%)	
No	163 (81.50)	-	37 (92.50)	
Yes	37 (18.50)	-	03 (7.50)	
Intolerance duration (months)	12-92	-	12-92	
mean ± SD	9.95 ± 22.69	-	49.73 ± 24.43	
Median	0	-	52	
Systemic diseases	n (%)	n (%)	n (%)	
No	190 (95.00)	153 (95.63)	37 (92.50)	
Yes	10 (5.00)	07 (4.37)	03 (7.50)	
Use of medication	n (%)	n (%)	n (%)	
No	188 (94.00)	155 (96.88)	33 (82.50)	
Yes	12 (6.00)	05 (3.12)	07 (17.50)	
Dmft	n (%)	n (%)	n (%)	
0	118 (59.00)	105 (65.63)	13 (32.50)	
>=1	82 (41.00)	55 (34.37)	27 (67.50)	< 0.001*
mean ± SD	1.01 ± 1.69	0.83 ± 1.60	1.75 ± 1.84	
Median	0	0	1	< 0.001*
Treatment need				
0	123 (61.50)	110 (68.75)	13 (32.50)	
>=1	77 (38.50)	50 (31.25)	27 (67.50)	< 0.001*
mean ± SD	0.88 ± 1.63	0.71 ± 1.62	1.58 ± 1.50	
Median	0	0	2	< 0.001*

CMPA: Cow's milk protein allergy; LI: Lactose intolerance; SD: standard deviation; *Significant difference between groups (p < 0.001).

The prevalence of caries in 5-to-8-year-old children with CMPA or LI was 67.50% and the mean dmft index was 1.75. Thirteen (32.50%) children were caries-free, without any carious lesions, tooth loss due to caries, or tooth restorations (Table 1). The mean number of decayed teeth amounted to 1.30, accounting for 74.29% of the dmft index. The distribution of dmft and components was not normal (Table 2).

Furthermore, 67.50% of the population with CMPA or LI required dental treatment but, on average, only 1.58 teeth required treatment (Table 1). There were no treatment needs for prosthetic crown, facet restorations, pulp treatment, and tooth extractions. Restorations of a single facet represented 77.85% of total treatment needs (Table 3).

FFQ results

Milk-based products consumed by children included whole milk, semi-skimmed milk, and

Table 2. Distribution of decayed, indicated extraction, filled components and dmft index in children with CMPA or LI (n = 40). Paraná, Southern Brazil, 2018.

Statistics	Decayed	Missing	Filled	dmft	Zero dmft
Mean	1.30	0.0	0.45	1.75	-
Standard deviation	1.40	0.0	1.30	1.84	-
%	74.29	0.0	25.71	100.0	32.50
Minimum	0.0	0.0	0.0	0.0	-
25% Quartile	0.5	0.0	0.5	0.0	-
Median	1.0	0.0	0.0	1.0	-
75% Quartile	2.0	0.0	0.5	2.5	-
Maximum	6.0	0.0	7.0	7.0	-

CMPA: Cow's milk protein allergy; LI: Lactose intolerance.

Table 3. Dental treatment need in children with CMPA or LI (n = 27). Means (in teeth) per individual, standard deviation, percentage rates, and sum. Paraná, Southern Brazil, 2018.

Statistics	Restoration	Restoration	Total	Zero ITN
	(one surface)	(two surfaces or more)		
Mean	1.23	0.35	1.58	-
SD	1.33	0.74	1.50	-
%	77.85	22.15	100.0	32.50
Sum	49	14	63	-

CMPA: Cow's milk protein allergy; LI: Lactose intolerance; SD: standard deviation.

skimmed milk; plain yogurt or fruit yogurt; lactose-free milk (LFM); and soy milk fruit juice (SJ). LFM and SJ had the highest consumption by children with CMPA, representing 65.00% and 40.00%, respectively (Table 4).

Table 4 shows the differences in consumption patterns between children with and without CMPA/LI. As expected, allergic or lactose-intolerant children consumed milk-based foods less frequently and replacement foods (LFM) more frequently than did those without CMPA or LI ($p < 0.001$). High or moderate consumption of foods such as chocolate milk, whole soy milk, soy milk powder, soy yogurt, chocolate soy milk, and other types of milk was not higher than 15% between the groups.

Association between oral health status and food consumption

The prevalence of dental caries, treatment needs, and dmft and ITN indices were compared to health conditions in three different ways. The first one consisted of the analysis of caries incidence and of treatment needs, classified as either absent (dmft/ITN = 0) or present (dmft/ITN \geq 1). The second one consisted in testing caries severity calculated by the mean dmft and ITN indices. The statistical analysis revealed a significant association between the prevalence of caries and treatment needs and between the dmft and ITN indices (Table 1). Children with CMPA/LI had a higher caries prevalence rate and need for treatment when compared to those without such health conditions ($p < 0.001$). The third type of analysis consisted in testing oral health status calculated by the mean dmft and ITN indices with regard to the foods most frequently consumed by children with and without CMPA/LI. No statistically significant difference was detected between the dmft index and the milk-based products most frequently consumed by children with CMPA/LI. However, a higher ITN index ($p < 0.005$) was observed for children who consumed soy milk fruit juice. This finding is related to treatment needs, which were 3.5 times greater when children with CMPA/LI with a high food intake were compared to those children without these types of food intolerance (Table 4).

Table 4. Frequency of food intake of children's formulas (n=200). Paraná, Southern Brazil, 2018.

Food groups	Total (n = 200)	Children without CMPA + LI (n = 160)	Children with CMPA + LI (n = 40)	p-value
WM/SSM/SM	n (%)	n (%)	n (%)	
High	117 (58.50)	113 (70.63)	04 (10.00)	< 0.001*
Moderate	42 (21.00)	29 (18.12)	13 (32.50)	
Low	41 (20.50)	18 (11.25)	23 (57.50)	
	mean ± SD	mean ± SD	mean ± SD	
dmft (high)	0.79 ± 1.58	0.78 ± 1.60	1.25 ± 0.96	
	Median	Median	Median	
	0	0	1.5	0.110
	mean ± SD	mean ± SD	mean ± SD	
Treatment need (high)	0.72 ± 1.67	0.68 ± 1.67	1.75 ± 1.26	
	Median	Median	Median	
	0	0	2	0.027*
PY/FY	n (%)	n (%)	n (%)	
High	17 (8.50)	16 (10.00)	01 (2.50)	
Moderate	89 (44.50)	72 (45.00)	17 (42.50)	0.228
Low	94 (47.00)	72 (45.00)	22 (55.00)	
	mean ± SD	mean ± SD	mean ± SD	
dmft (high + mild)	0.99 ± 1.74	0.77 ± 1.69	2.06 ± 1.66	
	Median	Median	Median	
	0	0	2	< 0.001*
	mean ± SD	mean ± SD	mean ± SD	
Treatment need (high + mild)	0.92 ± 1.91	0.72 ± 1.92	1.89 ± 1.60	
	Median	Median	Median	
	0	0	2	< 0.001*
LFM	n (%)	n (%)	n (%)	
High	37 (18.50)	11 (6.88)	26 (65.00)	< 0.001*
Moderate	04 (2.00)	01 (0.62)	03 (7.50)	
Low	159 (79.50)	148 (92.50)	11 (27.50)	
	mean ± SD	mean ± SD	mean ± SD	
dmft (high)	1.65 ± 1.87	0.82 ± 0.87	2.00 ± 2.08	
	Median	Median	Median	
	1	1	2	0.129
	mean ± SD	mean ± SD	mean ± SD	
Treatment need (high)	1.41 ± 1.57	0.64 ± 1.03	1.73 ± 1.66	
	Median	Median	Median	
	1	0	2	0.041*
SJ	n (%)	n (%)	n (%)	
High	70 (35.00)	54 (33.75)	16 (40.00)	0.578
Moderate	37 (18.50)	23 (14.37)	14 (35.00)	
Low	93 (46.50)	83 (51.88)	10 (25.00)	
	mean ± SD	mean ± SD	mean ± SD	
dmft (high)	2.09 ± 2.27	1.87 ± 2.23	2.81 ± 2.32	
	Median	Median	Median	
	1	1	3	0.115
	mean ± SD	mean ± SD	mean ± SD	
Treatment need (high)	1.87 ± 2.28	1.69 ± 2.42	2.50 ± 1.67	
	Median	Median	Median	
	1	1	3	0.017*

CMPA: Cow's milk protein allergy; FY: fruit yogurt; LFM: lactose-free milk; LI: Lactose intolerance; PY: plain yogurt; SD: standard deviation; SJ: soy milk fruit juice; SM: skimmed milk; SSM: semi-skimmed milk; *Significant difference between groups (p < 0.05).

Discussion

The present study on dental caries, treatment needs, and their relationship with medical and nutritional factors in children with CMPA or LI reveals high caries prevalence and dental treatment rates. However, these needs are easily solved through clinical procedures of low complexity.

Globalization and neoliberal policies adopted by large multinational food manufacturers have led to the higher and early consumption of processed food by children.²⁶ Consumption trends emerge mainly among children with special allergic and food intolerance conditions. This provides new room for the development of epidemiological studies for the identification of population groups at high risk for dental caries. Since the pattern of caries development has undergone several changes in an era characterized by industrialized food, in-depth studies are required so that children with special health needs and the respective stages of the disease can be followed up. This would contribute towards the establishment of prevention policies, health promotion, and control and treatment of the main oral diseases.

Although dental caries is the oral disease most widely investigated worldwide, most of the research focuses on children without CMPA/LI. Specific data on this population are lacking, even in the case of industrialized countries. In fact, the few epidemiological studies at hand refer to the consumption of soy-based foods¹⁸ and of lactose-free milk.¹⁹

By comparing the results of the present research to those of a study of children without CMPA/LI in government-run schools in Araçatuba, Brazil, in 2010,²⁷ caries prevalence (67.50%) was higher in this study than the rate (44.70%) obtained for 4-to-6-year-old children in that study.

Mean dmft rates in the same study for 5- and 6-year-old children were respectively 1.65 and 1.72, lower than the 1.75 index observed in the current analysis. Results are worse when compared to the national data from SB Brasil 2010.²⁸ In the case of 5-year-old children, caries prevalence was as high as 83.62%, with a mean dmft index of 2.43. It should be underscored that the current research evaluated 5-to-8-year-old children from a private school, who,

allegedly, have a better socioeconomic background and higher parental schooling than those in government-run schools.

Dental caries was the main component of the dmft index in children with CMPA/LI, which amounted to 74.29%, corroborating the 80.20% rate obtained by the National Research on Oral Health of Brazilian populations.²⁸ Results demonstrate that these children did not have access to dental services.

Also, results show that seven children (17.50%) with CMPA/LI and caries had a dmft index ≥ 4 . These children make up a representative group which needs dental treatment, or rather, they constitute an epidemiological polarization group. These findings reveal that children with CMPA/LI need prevention programs for caries and more dental care.

The current study evidenced an association between dental caries and treatment needs for primary dentition and CMPA/LI. There was, however, no significant association between dental caries and the large consumption of foods, lactose-free milk, and soy milk fruit juice by children with CMPA/LI. In fact, Carvalho et al.¹⁸ reported a relationship between dental fluorosis and LI in a group of 26 kindergarten children aged 4-6 years ($p < 0.05$), but no association with soy-based products consumed by these children.

Contrastingly, Cagetti et al.¹⁹ detected a 42.31% caries prevalence in schoolchildren aged 6-8 years and associated the ingestion of lactose-free milk with moderate caries presence ($p = 0.02$), benchmarked by the International Caries Assessment and Detection System (ICDAS). Therefore, further epidemiological studies of children with CMPA/LI from different countries and including other samples should be performed to evaluate the different risks for oral disease among these children.

The oral health of children with CMPA/LI proved to be worse when compared to that of children without CMPA/LI due to dietary restrictions on an important source of calcium (cow's milk) and to the replacement of industrialized soy-based foods with sugar-rich and low pH products, which may potentiate the enamel demineralization in the primary dentition,¹³ in addition to tooth erosions.²⁹ However, one should bear in mind the current limited knowledge on the epidemiological pattern of caries in children allergic

to other types of food and whose food consumption is hypothetically different from that of children with CMPA/LI. Another limitation in the present study was the use of a validated FFQ, rarely used in dentistry, without further details on potentially cariogenic foods.

The results highlight the importance of dental caries prevention in children with CMPA/LI. Prevention programs should also be targeted at other specific groups. The best strategy relies on different diagnostic, cultural, economic, and geographic factors, among others. Some strategies could include the use of fluoride, chlorhexidine-based mouth rinses, and sealants, in addition to motivational, behavioral, and collective activities. The early identification of groups at high risk for dental caries in prevention programs should be enhanced,^{27,30,31} combined with the

establishment of public policies for caries reduction, increasing the access to oral health services.³²

Conclusions

Prevalence and severity of dental caries and treatment needs in primary dentition in children were associated with CMPA and LI. The consumption of replacement foods by children with CMPA/LI did not cause the development of carious lesions. However, this special health condition should be taken into account when planning cure, prevention, and educational programs on oral health for children within the age bracket investigated herein.

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