Hindawi
BioMed Research International
Volume 2021, Article ID 9992451, 10 pages
https://doi.org/10.1155/2021/9992451

Research Article

The Association between Nutritional Alterations and Oral Lesions in a Pediatric Population: An Epidemiological Study

Angela Pia Cazzolla,[1] **Michele Di Cosola**,[1] **Andrea Ballini**,[2,3] **Luigi Santacroce**,[4,5] **Roberto Lovero**,[6] **Nunzio Francesco Testa**,[1] **Vitantonio Lacarbonara**,[7] **Annarosa De Franco**,[7] **Giuseppe Troiano**,[1] **Stefania Cantore**,[4] **Mariasevera Di Comite**,[7] **Riccardo Nocini**,[8] **Lorenzo Lo Muzio**,[1] **Vito Crincoli**,[7] **and Mario Dioguardi**[1]

[1]*Department of Clinical and Experimental Medicine, Università degli Studi di Foggia, Foggia 71122, Italy*
[2]*School of Medicine, University of Bari "Aldo Moro", Bari 70124, Italy*
[3]*Department of Precision Medicine, University of Campania "Luigi Vanvitelli", Naples 80138, Italy*
[4]*Department of Interdisciplinary Medicine, University of Bari "Aldo Moro", Bari 70124, Italy*
[5]*Department of Clinical Disciplines, School of Technical Medical Sciences, University of Elbasan "A. Xhuvani", Elbasan 3001, Albania*
[6]*AOU Policlinico Consorziale di Bari-Ospedale Giovanni XXIII, Clinical Pathology Unit, Policlinico University Hospital of Bari, Bari 70124, Italy*
[7]*Department of Basic Medical Sciences, Neurosciences and Sensory Organs, University of Bari "Aldo Moro", Bari 70124, Italy*
[8]*Section of Ear Nose and Throat (ENT), Department of Surgical Sciences, Dentistry, Gynecology and Pediatric, University of Verona, Verona 37126, Italy*

Correspondence should be addressed to Andrea Ballini; andrea.ballini@me.com
and Stefania Cantore; stefaniacantore@pec.omceo.bari.it

Received 30 September 2021; Accepted 21 October 2021; Published 29 October 2021

Academic Editor: Iole Vozza

The oral conditions of an individual are the result of different factors, including the subject's genotype, oral hygiene habits, the type of diet, and lifestyle, such as smoking. Nutrition in the first years of life can affect dental health for a long time. To prevent mouth diseases, it is also important to eliminate unfavorable eating behaviour and to amplify protective ones. Eating habits, especially in pediatric age, are an easily modifiable and controllable factor, and diet, in addition to influencing the health of the oral cavity, plays a fundamental role in systemic health. Indeed, a sugar-rich diet can lead to conditions, such as diabetes, being overweight, and obesity. The present research was an epidemiological study, with the aim of highlighting some of the associations between nutrition and oral health. In particular, we studied those lesions of hard and soft tissues that are diagnosed most frequently by dentists: caries, enamel hypoplasia, periodontal disease, and aphotoxic lesions and their associations with nutritional deficiencies and excesses including proteins, vitamin A, vitamin D, B vitamins, and iron and calcium minerals. To perform this study, we recruited 70 patients from the pediatric and orthodontic clinics, aged between 3 and 15 years (y), with mean age of 10.4 y.o. The study was conducted by providing a questionnaire to pediatric patients' (supported from their parents or guardians) on individual eating habits, followed by an accurate oral cavity specialistic examination. The nutritional data were processed by using Grana Padano Observatory (OGP) software, freely provided online by the OPG. The statistical tests performed were the chi-square (χ^2) for independence, and Cramér's V test was used to evaluate the associations between eating habits and oral pathologies. The results showed that certain nutritional vitamin deficiencies and nutritional excesses were associated with definite oral pathologies.

1. Introduction

The oral conditions of an individual are the result of various factors, such as the subject's genotype, oral hygiene habits (i.e., toothbrushing), type of diet, and any smoking habits [1–3]. Unhealthy eating habits adversely affect both oral and general health. Nutrition in the early years of life can influence long-term dental health [4–7]. Foods that are harmful to general health can also damage teeth and *vice versa*. Research has been focusing on the effect of nutrition on mucous membranes and hard dental tissues, which can be a systemic effect or a local effect, such as the effect of acidic foods and drinks on the teeth, which can be responsible for dental erosion in patients with good oral hygiene [8–11]. Changing one's eating habits and lifestyle can lead to the improvement of oral and systemic conditions [12–15].

To prevent mouth diseases, it is, therefore, advisable to change the modifiable factors, eliminating unfavorable ones and amplifying the protective ones. Eating habits represent an easily modifiable and controllable factor, knowing that diet, in addition to influencing the health of the oral cavity, plays a fundamental role in systemic health, acting also in the autologous self-renewal stem cell niche, related to the oral mucous membrane trophism [16, 17]. It is well known that a diet rich in sugars can lead to conditions, such as diabetes, being overweight, and obesity [18]. The present research was an epidemiological study, with the aim of highlighting some of the associations between nutrition and oral health.

In particular, our attention was directed towards those lesions of hard and soft tissues more frequently diagnosed by a dental practitioner: caries, enamel hypoplasia, periodontal disease, and aphthous lesions. The nutrients we assessed for excesses or deficits in pediatric patients, based on the frequency of intake of certain foods, were proteins, vitamin A, vitamin D, vitamins of group B, and the minerals iron and calcium. Our main questions were as follows: (1) "What eating habits can influence the onset of these statuses?" and (2) "At what point can a correct diet act on the maintenance of a good trophism of the oral mucous membranes and on the formation and safeguarding of dental structures?"

2. Materials and Methods

This research was conducted in collaboration with Elbasan University "A. Xhuvani" (School of Technical Medical Sciences), Elbasan, Albania, a dental community cabinet (Sorriso & Benessere—Ricerca e Clinica SRL, Bari, Italy), the University of Bari Aldo Moro (Italy), and the University of Foggia (Italy).

To perform this study, we recruited 70 pediatric patients from the pediatric and orthodontic private practice clinics. The Institutional Ethics Committee of the Faculty of Technical Medical Sciences of Elbasan "Aleksandër Xhuvani" approved the application to conduct the clinical trial in the faculty (protocol identification: INTL_ALITCOOP/DentPath/2020_SLK). Informed consent was obtained from all subjects' parents or guardians involved in the study. Written informed consent was obtained from the patients' parents or guardians to publish this paper.

The inclusion criteria were as follows:

(i) Age from 3 to 15 years, with a mean age of 10.4 years, a standard deviation of 2.75, and a median (value that leaves 50% on the left and 50% on the right of a series of data sorted in a nondecreasing way) of 10

(ii) Gender: both male and female

(iii) The absence of situations requiring special diets

The exclusion criteria include all situations that required specific diets, including diabetes and hereditary metabolic diseases such as phenylketonuria, glycogenosis, galactosemia, celiac disease, severe food intolerances, and chronic inflammatory bowel diseases.

During the first phase of the study, we administered a questionnaire to patients that inquired about their eating habits. To obtain more reliable answers, we typically asked for the help of the parents. For the purposes of this research, the software freely available online, following registration at the website http://www.osservatorio.granapadano.it (OGP), was used (i) to evaluate if the patients' food intake was appropriate and (ii) to provide them personalized nutritional advice, highlighting any nutritional deficiencies or excesses caused by their ordinary diet [19].

The first phase, that of the interview, allowed an active healthcare professional- (dentist) patient relationship, strengthened by the emotional elements linked to nutrition (nourishing means, first of all, "taking care" of someone), and the subsequent phase of delivery of the press of the nutritional advice involved communicating things never said before, and do this in a way where the patient feels empathy from the healthcare professional, facilitated by the "counseling" approach. Through this, thanks to the healthcare professional, the patient becomes the protagonist of the change process, acquiring awareness of their own eating habits and lifestyle. This was a useful and powerful tool of improving compliance and achieving expected results more easily.

For the calculation of nutritional needs, the software refers to age groups expressed as follows:

(i) From 3 to 6 years, male and female

(ii) From 7 to 10 years, male and female

(iii) From 11 to 15 years, male and female

(iv) From 11 to 15 years, female

Data collection was conducted with the help of an electronic questionnaire to evaluate the frequency of weekly or, alternatively, monthly intake of the most common foods of the interviewee's diet, whose nutrient content was "weighed."

The data collected by the questionnaire were as follows:

(i) Essential personal data for the inclusion of the subject within a specific cluster

(ii) The weight and height for calculating the body mass index (BMI)

(iii) The abdominal circumference (the weight, height, and abdominal circumference data can be reported by the subject or detected by the healthcare professional, and the software automatically checks "therefore if the healthcare professional decides to detect the data, the corresponding item must be ticked")

(iv) Lifestyle data (hours spent close to television and/or at personal computer/notebook for free time, smoking habits, physical activity, etc.)

Before moving on to the analysis of individual foods, we asked for the weekly frequency of intake of certain food families (side dishes, fruits, dairy products, meats, and salami). The collected data were compared with those collected during the administration of the detailed questionnaire, in order to reduce the risk of underestimating/overestimating the consumption of relevant foods.

During the detailed interview, a number was inserted for each food that responds to weekly or monthly assumptions; if the food in question was not taken, the corresponding space was left blank. The single intake refers to the quantity of food, expressed in grams, which represents the standard portion for age and sex, which was automatically extrapolated from the dedicated software. When the questionnaire reports more than one food in the same row (for example, beans, lentils, fava beans, chickpeas, and boiled/canned cooked soybeans), it was necessary to sum the intake of the individual foods and report their total value in the box with the relative frequency.

Once the data were acquired through the questionnaire, it was possible to proceed to the oral cavity specialist pathological anamnesis. We asked patients if they suffered from particular mucous diseases, almost always not detectable at the time of the visit, as in the case of vesicular-bullous lesions or aphthous lesions. We investigated the onset of any burning or painful symptoms associated with the ingestion of particular foods and the possible remission of the symptoms when avoiding the intake.

The third step consisted of the objective examination of the patients' oral cavity to assess the presence of caries, earlier restorative treatments, endodontic therapies, dental erosions, missing teeth, enamel hypoplasia, and calcifications, as well the gingival status and the presence of plaque/calculus.

Therefore, the information available for each patient included the following:

(i) The nutritional status

(ii) The nutritional deficiencies or excesses

(iii) The clinical history

(iv) The current presence of caries, already restored teeth, enamel hypoplasia, enamel erosion, gingivitis, and periodontal disease

(v) Information reported on the possible appearance of aphthous lesions

We collected the data acquired through the OGP software, the anamnesis, and the physical examination, and, in particular, for each of the 70 patients, we assessed the presence or absence of the following:

(i) Excesses of proteins, carbohydrates, lipids, saturated fats, and cholesterol

(ii) Deficiencies of carbohydrates, lipids, vitamin C, vitamin A, vitamin D, calcium, iron, and omega 3

(iii) The presence of four types of lesions: caries, gingivitis, enamel hypoplasia, and aphthosis

The above elements were the variables available to us to conduct a study on the association between nutritional alterations and oral lesions.

The statistical analysis between the variables was performed with the chi-square test (χ^2) for the evaluation of the significance of the association or independence. The degree of association between the nominal variables was verified with Cramér's V index (C).

3. Results

The results showed the following deficiencies in the diet (expressed as percentages): calcium (67%), vitamin D (66%), iron (56%), vitamin A (30%), carbohydrates (23%), omega 3 (20%), lipids (17%), and vitamin C (16%). The excessive amounts of nutrients introduced with diet were cholesterol (64%), saturated fats (63%), proteins (58.56%), lipids (44%), and carbohydrates (20%) (Tables 1(a)–1(c)).

As reported in Table 2, it shows the average ages, and most of the alterations (9 out of 13) were present at a slightly lower average age. The excesses of carbohydrates and saturated fats and the deficiencies of carbohydrates, lipids, vitamin C, vitamin D, calcium, iron, and omega 3 were present in subjects with a lower average age compared with those who were not characterized by such alterations. Only the excesses of proteins, lipids, and cholesterol and deficiency of vitamin A were found in patients with a higher average age compared to patients who did not have these alterations.

From this, we consider that the diet tended to improve with advancing growth. Clearly, we are talking about children who, having an age greater than 3 years, begin to select foods of their preference, avoiding quality (Table 3).

Regarding the sample's oral lesions, the following were found:

(i) 50% had caries

(ii) 34% had periodontal disease, represented by mild or moderate gingivitis

(iii) 33% had hypoplasia of the enamel

(iv) 20% reported the more or less frequent onset of canker sores

Table 1

(a) Population and distribution of subjects (total = 70), with an excess of each of the variables considered

Excess	n	%
Protein	41	58.6
Lipids	31	44.3
Carbohydrates	14	20.0
Saturated fats	44	62.9
Cholesterol	45	64.3

(b) Population and distribution of subjects (total = 70), with a deficiency of each of the variables considered

Deficiency	n	%
Carbohydrates	16	22.9
Lipids	12	17.1
Vitamin C	4	5.7
Vitamin A	21	30.0
Vitamin D	46	65.7
Calcium	47	67.1
Iron	39	55.7
Omega 3	14	20.1

(c) Population and distribution of subjects (total = 70), with a deficiency of each of the variables considered

Oral lesions	n	%
Caries	35	50.0
Gingivitis	24	34.2
Hypoplasia	23	32.9
Aphthae	14	20.0

The rejection region for the χ^2 test of independence (Table 4), between the explanatory variable (presence or absence of nutritional alteration) and dependent variable (presence or absence of a lesion), showed dependence between the following:

(i) Caries and excess lipids and carbohydrates

(ii) Periodontal disease and excess saturated fats and carbohydrates

(iii) Periodontal disease and deficient vitamin C and iron

(iv) Enamel hypoplasia and deficient vitamin D

(v) Aphthae and deficient vitamin A

Through Cramér's V index, these associations were classified based on their degree of significance (Table 5).

(1) Vitamin A deficiency and canker sores ($C = 0.37$)

Table 2

(a) Ratio of the number of individuals with the presence (P) or absence (A) of excesses for each nutritional variable into the sample size (70 patients). Upper (U.L.) and lower (L.L.) limits can differ, within the sample population

Excess	A (n)	P (n)	U.L.	L.L.
Protein	0.41	0.59	0.70	0.47
Lipids	0.56	0.44	0.56	0.33
Carbohydrates	0.80	0.20	0.29	0.11
Saturated fats	0.71	0.63	0.74	0.52
Cholesterol	0.36	0.64	0.76	0.53

(b) Ratio of the number of individuals with the presence (P) or absence (A) of deficiencies for each nutritional variable into the sample size (70 patients). Upper (U.L.) and lower (L.L.) limits can differ, within the sample population

Deficiency	A (n)	P (n)	U.L.	L.L.
Carbohydrates	0.77	0.23	0.33	0.13
Lipids	0.83	0.17	0.26	0.08
Vitamin C	0.94	0.06	0.14	0.02
Vitamin A	0.70	0.30	0.41	0.19
Vitamin D	0.34	0.66	0.77	0.55
Calcium	0.33	0.67	0.78	0.56
Iron	0.44	0.56	0.67	0.44
Omega 3	0.80	0.20	0.29	0.11

(c) Ratio of the number of individuals with the presence (P) or absence (A) of specific oral lesions to the sample size (70 patients). Upper (U.L.) and lower (L.L.) limits can differ, within the sample population

Oral lesions	A (n)	P (n)	U.L.	L.L.
Caries	0.50	0.50	0.62	0.38
Gingivitis	0.66	0.34	0.45	0.23
Hypoplasia	0.67	0.33	0.44	0.22
Aphthae	0.80	0.20	0.29	0.11

(2) Excess carbohydrates and caries ($C = 0.35$)

(3) Vitamin C deficiency and periodontal disease ($C = 0.34$)

(4) Iron deficiency and periodontal disease ($C = 0.28$)

(5) Excess lipids and caries ($C = 0.258$)

(6) Excess of saturated fat and periodontal disease ($C = 0.254$)

(7) Carbohydrate deficiency and periodontal disease ($C = 0.251$)

(8) Vitamin D deficiency and enamel hypoplasia ($C = 0.24$)

Table 3: Patients' mean age in the presence (P) or absence (A) of each nutritional alterations and oral lesions. The table also highlights whether the alteration characterizes a trail of greater or lower age (*P* major/minor).

	A	P	*P* major/minor
Excess			
Protein	9.93	10.12	+0.19
Lipids	9.31	10.97	+1.66
Carbohydrates	10.09	9.86	-0.23
Saturated fats	10.08	10.02	-0.05
Cholesterol	9.92	10.11	+0.19
Deficiency			
Carbohydrates	10.09	9.88	-0.22
Lipids	10.26	9.00	-1.26
Vitamin C	10.18	7.75	-2.43
Vitamin A	9.98	10.19	+0.21
Vitamin D	10.42	9.85	-0.57
Calcium	10.48	9.83	-0.65
Iron	10.10	10.00	-0.10
Omega 3	10.57	7.93	-2.64
Oral lesions			
Caries	10.20	9.89	-0.31
Gingivitis	9.98	10.17	+0.19
Hypoplasia	10.11	9.91	-0.19
Aphthae	10.05	10.00	-0.05

4. Discussion

The results obtained in this study regarding the association between nutritional alterations and oral manifestations have found confirmation in various studies [19–21]. Several studies have shown the existence of an association between nutritional alterations and tooth decay: studies that have evaluated the distribution of the body mass index (BMI) and the D(3+4)MFT index in a sample of children and have compared the different regression models by analyzing the association between these two indices [22–24]. Chen et al. in a cross-sectional study stated that an excess of fats does not predispose to caries [25], data confirmed by subsequent studies [26–28].

Bowen, on the other hand, reported how the significant presence of fats in the diet influenced cariogenicity, as fats would increase the clearance of sugars in the oral environment. It would also be conceivable that many fatty acids would exhibit a powerful antibacterial effect [24]; also, changes in the lipid levels and fatty acid composition could, therefore, be associated with caries development [29–32]. Earlier studies confirmed the association between caries and a sugar diet in accordance with the results of our study [33–36]. Gerdin et al. in a study aimed at evaluating the association between dental caries, body mass index, and socioeconomic status in Sweden concluded that the prevalence of being overweight and having caries was (weakly) associated in Swedish children [33].

Murty et al. reported in their study that saliva played a very important role in the prevention and development of tooth decay in enamel [35]. The study involved a comparison between two samples, one with caries-resistant subjects and the other with caries-sensitive subjects, showing that lipid concentration in the parotid saliva was higher in subjects with caries susceptibility [35].

Special cases are represented by the baby bottle syndrome: in the context of pathologies affecting deciduous teeth, we refer to the baby bottle tooth decay syndrome, which derives from incorrect use of the bottle [37–39]. For instance, letting the child fall asleep with the bottle by sucking milk or other sweet substances, or leaving the child for hours with a pacifier soaked in cariogenic substances (i.e., honey or sugar), is strongly discouraged as it often causes the formation of caries so extensive as to reduce the tooth to a small dark stump with consequent, painful abscesses, leading in this way to extracting the decayed dental elements. Statistically, children under 3 years of age are the most affected (in particular the incisor area) [40–43].

For the association between canker sores and vitamin A deficiency, the control function of vitamin A in the keratinization, maturation, and hydration of mucous membranes and skin was implicated [44–47]. Various studies confirm the association between aphthosis and nutritional deficiencies; however, they principally concerned deficiencies of iron, folate, and vitamins of the B group [48–51].

In the literature, we did not find clinical studies in which the association between the onset of aphthosis and the low vitamin A diet was highlighted [52–55]. In our findings, this association was established. Only Scully and Boyle describe, in 1992, in a review, the role of vitamin A in the prevention of potentially malignant lesions by indicating the protective effects but do not describe their pathogenic mechanisms [56].

Associations between vitamin C and D deficit and periodontal disease are described in the literature [56–59]. In our study, only four patients demonstrated a deficit of vitamin C (contained deficit), but all had a sustained degree of gingivitis [60, 61]. These were patients who had undergone more than one oral hygiene session due to the increased susceptibility to plaque buildup and inflammatory responses of the gums that led to edema and bleeding on probing more easily [62–64].

Regarding the association between a high-fat diet and periodontal disease, we can reiterate that, as adipose tissue is a source of inflammatory cytokines, an increase in body fat increases the risk of an increased inflammatory response in periodontitis [65, 66]. Several studies have shown the association between obesity and periodontitis [67–69].

Obesity is characterized by abnormal or excessive deposition of fat in the adipose tissue. The consequences go far beyond negative metabolic effects on health, causing an increase in oxidative stress, which leads not only to endothelial dysfunction but also to negative effects in relation to periodontitis, due to the increase in the inflammatory cytokines that are produced [70]. Thus, obesity appears to participate in the multifactorial phenomenon of the causality of

Table 4: Chi-square test. Values rejecting the null hypothesis of independence supportive alternative association (∗).

(a)

Excess	Protein	Lipids	Carbohydrates	Saturated fats	Cholesterol
Caries	0.0589	4.6898*	8.9286*	0.2448	0.5600
Gingivitis	0.2323	0.0355	0.2536	4.5335*	0.0507
Hypoplasia	3.3226	0.3690	1.0361	0.0580	0.0130
Aphthae	0.5299	1.7514	1.8080	0.0153	0.0000

(b)

Deficiency	Carbohydrates	Lipids	Vit. C	Vit. A	Vit. D	Calcium	Iron	Omega 3
Caries	0.0000	3.6207	1.0606	0.0680	2.2826	1.6189	2.8371	3.2143
Gingivitis	4.4410*	0.3502	8.1313*	0.4348	1.3977	0.0038	5.5054*	0.5707
Hypoplasia	0.5804	0.0015	0.5651	0.2498	4.3395*	1.9193	0.1740	0.0648
Aphthae	1.6406	1.6092	0.0663	9.7959*	0.0159	1.0361	3.7055	2.7009

Table 5: Cramér's V index values (∗ indicates significant association).

(a)

Excess	Protein	Lipids	Carbohydrates	Saturated fats	Cholesterol
Caries	0.0290	0.2588*	0.3571*	0.0591	0.0894
Gingivitis	0.0576	0.0225	0.0602	0.2545*	0.0269
Hypoplasia	0.2179	0.0726	0.1217	0.0288	0.0136
Aphthae	0.0870	0.1582	0.1607	0.0148	0.0000

(b)

Deficiency	Carbohydrates	Lipids	Vit. C	Vit. A	Vit. D	Calcium	Iron	Omega 3
Caries	0.0000	0.2274	0.1231	0.0312	0.1806	0.1521	0.2013	0.2143
Gingivitis	0.2519*	0.0707	0.3408*	0.0788	0.1413	0.0073	0.2804*	0.0903
Hypoplasia	0.0911	0.0046	0.0899	0.0597	0.2490*	0.1656	0.0499	0.0304
Aphthae	0.1531	0.1516	0.0308	0.3741*	0.0150	0.1217	0.2301	0.1964

periodontitis through an increase in the production of reactive oxygen species [70, 71].

Another association that emerged from our study was between a low-iron diet and periodontal disease. Enhos et al. led a study aimed at assessing the periodontal health status in patients with iron deficiency anemia, through the detection of ferritin levels in the crevicular fluid before and after periodontal therapy and concluded that iron deficiency was not a factor of direct risk for periodontal disease. There are, however, many other lesions associated with iron deficiency, such as atrophy of the lingual papillae, atrophic glossitis, angular cheilitis, and hyposalivation [72].

Regarding the association we found between periodontal disease and the low introduction of carbohydrates, the literature does not provide us with much data. Merchant et al.'s study showed an inverse correlation between the intake of whole grains and periodontitis [73]. Finally, regarding the last association between vitamin D deficiency and enamel hypoplasia, we can confirm this strong association widely described in the literature [74]. Vitamin D is strongly implicated as it is a direct protagonist of the deposition of calcium and phosphorus in the bones and teeth [75–78].

Throughout physical/oral examinations and the study of each patient's medical records, we collected data regarding the presence of oral lesions.

Statistical analysis confirmed many associations already reported in literature so far, introducing new original data. In this study, being a preliminary study, the results can be used as a baseline data for future studies with similar study design. For the issues related to "excess carbohydrates and caries," "vitamin C deficiency and periodontal disease," and "vitamin D deficiency and enamel hypoplasia," the associations already established were confirmed [79–82]. Therefore, in these three specific investigations, our findings have

the role only to strengthen and confirm current concepts. In contrast, the issues related to "vitamin A deficiency and canker sores," "iron deficiency and periodontal disease," and "carbohydrate deficiency and periodontal disease," more attractive results are introduced. In particular, association between "vitamin A deficiency and canker sores" not only confirmed but also showed a higher statistical significance. This could be due to the role that vitamin A plays in epithelialisation and keratinisation.

For the last association related to iron-periodontopathic deficiency, with regard to points "excess lipids and caries" and "excess of saturated fats and presence of periodontal disease," the relationships are according to literature reports [83–85]. However, studies of longer duration with crossover study design and wider sample size would have been more authenticating as it eliminates the bias of viable host.

5. Conclusions

The most relevant data emerging from the current research was the presence of an association between vitamin A deficiency and canker sores ($C = 0.37$) that has been not often described in scientific literature. The obtained results lead us to conclude that a correct and balanced diet, without excess and without nutritional deficiencies, contributes to the well-being of overall human body, including oral cavity, laying the fundamentals for proper tooth structure, maintaining the tropism of the mucosal membranes.

In addition, conclusions on an association of nutrient deficiency with periodontal disease cannot be assessed if the results are adjusted for comorbidity, such as smoking, diabetes mellitus, and other systemic diseases.

To produce conclusive evidence on the subject of this study, longitudinal cohort studies and follow-up randomized controlled trials are needed.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' Contributions

A.P.C, M.D.C., and V.C. were responsible for the concept and design. A.B., L.S., R.L., and S.C. were responsible for the acquisition, analysis, and interpretation of data. M.D., A.B., and S.C. drafted the manuscript. S.C., N.F.T., V.L., and A.D.F. conducted bibliographic research. M.D.C., L.L.M., V.C., and M.D. critically revised the manuscript for important intellectual content. G.T., M. Di Comite., and R.N. were responsible for the data interpretation and technical and material support. S.C., M.D.C., L.S., A.B., and L.L.M. were responsible for the supervision and final approval. All authors have read and agreed to the published version of the manuscript. Angela Pia Cazzolla, Michele Di Cosola, and Andrea Ballini contributed equally as co-first authors. Vito Crincoli and Mario Dioguardi contributed equally as co-last authors.

References

[1] R. L. Speirs and J. A. Beeley, "Food and oral health: 1," *Dental caries. Dent Update*, vol. 19, pp. 100–104, 1992.

[2] N. Cirulli, S. Cantore, A. Ballini et al., "Prevalence of caries and dental malocclusions in the apulian paediatric population: an epidemiological study," *European Journal Paediatric Dentistry*, vol. 20, no. 2, pp. 100–104, 2019.

[3] A. Ballini, M. Di Cosola, R. Saini et al., "A Comparison of manual nylon Bristle Toothbrushes versus thermoplastic elastomer toothbrushes in terms of cleaning efficacy and the biological potential role on gingival health," *Applied Sciences*, vol. 11, no. 16, p. 7180, 2021.

[4] A. S. Sham, L. K. Cheung, L. J. Jin, and E. F. Corbet, "The effects of tobacco use on oral health," *Hong Kong medical journal = Xianggang yi xue za zhi*, vol. 9, no. 4, pp. 271–277, 2003.

[5] J. L. Fried, "Women and tobacco: oral health issues," *Journal of dental hygiene: JDH*, vol. 74, no. 1, pp. 49–55, 2000.

[6] S. J. Meraw, I. Z. Mustapha, and R. S. Rogers 3rd., "Cigarette smoking and oral lesions other than cancer," *Clinics in Dermatology*, vol. 16, pp. 625–631, 1998.

[7] A. Itthagarun and S. H. Wei, "Chewing gum and saliva in oral health," *The Journal of Clinical Dentistry*, vol. 8, no. 6, pp. 159–162, 1997.

[8] R. Kazda, "Effects of smoking on the teeth and mouth cavity," *Wiener medizinische Wochenschrift (1946)*, vol. 144, no. 22-23, pp. 569-570, 1994.

[9] M. R. Darling and T. M. Arendorf, "Review of the effects of cannabis smoking on oral health," *International Dental Journal*, vol. 42, no. 1, pp. 19–22, 1992.

[10] R. M. Palmer, "Tobacco smoking and oral health," *British Dental Journal*, vol. 164, pp. 258–260, 1988.

[11] Z. L. Lee, W. Y. Gan, P. Y. Lim, R. Hasan, and S. Y. Lim, "Associations of nutritional status, sugar and second-hand smoke exposure with dental caries among 3- to 6-year old Malaysian pre-schoolers: a cross-sectional study," *BMC Oral Health*, vol. 20, p. 164, 2020.

[12] L. G. Freitas, M. A. P. Cortés, C. Stein, E. Cousin, D. D. Faustino-Silva, and J. B. Hilgert, "Dietary intake quality and associated factors in one year-old children seen by primary healthcare services," *Ciência & Saúde Coletiva*, vol. 25, pp. 2561–2570, 2020.

[13] M. Di Cosola, A. P. Cazzolla, I. A. Charitos, A. Ballini, F. Inchingolo, and L. Santacroce, "Candida albicans and oral carcinogenesis," *Journal of Fungi*, vol. 7, p. 476, 2021.

[14] A. N. Badavannavar, S. Ajari, K. U. S. Nayak, and S. Khijmatgar, "Abfraction: etiopathogenesis, clinical aspect, and diagnostic-treatment modalities: a review," *Indian Journal of Dental Research*, vol. 31, pp. 305–311, 2020.

[15] P. R. Kavitha, P. Vivek, and A. M. Hegde, "Eating disorders and their implications on oral health–role of dentists," *Journal of Clinical Pediatric Dentistry*, vol. 36, pp. 155–160, 2011.

[16] F. Posa, G. Colaianni, M. Di Cosola et al., "The myokine irisin promotes osteogenic differentiation of dental bud-derived MSCs," *Biology (Basel)*, vol. 10, no. 4, p. 295, 2021.

[17] I. A. Charitos, A. Ballini, S. Cantore et al., "Stem cells: a historical review about biological, religious, and ethical issues," *Stem Cells International*, vol. 2021, 11 pages, 2021.

[18] F. Lifshitz, P. L. Casavalle, N. Bordoni, P. N. Rodriguez, and S. M. Friedman, "Oral health in children with obesity or diabetes mellitus," *Pediatric endocrinology reviews: PER*, vol. 14, no. 2, pp. 159–167, 2016.

[19] D. Festi, A. Colecchia, S. Pini et al., "Development and application of a simple and powerful tool for nutrition and lifestyle education for the Italian general population by general practitioners and family paediatricians," *Mediterranean Journal of Nutrition and Metabolism*, vol. 2, pp. 139–144, 2009.

[20] P. Tramini, N. Molinari, M. Tentscher, C. Demattei, and A. G. Schulte, "Association between caries experience and body mass index in 12-year-old French children," *Caries Research*, vol. 43, pp. 468–473, 2009.

[21] T. Kennedy, C. Rodd, C. Daymont et al., "The association of body mass index and severe early childhood caries in young children in Winnipeg, Manitoba: A cross-sectional study," *Manitoba: A cross-sectional study. International journal of paediatric dentistry*, vol. 30, no. 5, pp. 626–633, 2020.

[22] A. Edalat, M. Abbaszadeh, M. Eesvandi, and A. Heidari, "The relationship of severe early childhood caries and body mass index in a group of 3- to 6-year-old children in Shiraz," *J Dent (Shiraz)*, vol. 15, no. 2, pp. 68–73, 2014.

[23] B. Sheller, S. S. Churchill, B. J. Williams, and B. Davidson, "Body mass index of children with severe early childhood caries," *Pediatric Dentistry*, vol. 31, no. 3, pp. 216–221, 2009.

[24] W. H. Bowen, "Food components and caries," *Advances in Dental Research*, vol. 8, pp. 215–220, 1994.

[25] W. Chen, P. Chen, S. C. Chen, W. T. Shih, and H. C. Hu, "Lack of association between obesity and dental caries in three-year-old children," *Zhonghua Minguo Guo Xiao Er Ke Yi Xue Hui Za Zhi*, vol. 39, pp. 109–111, 1998.

[26] K. Swaminathan, V. Anandan, H. SelvaKumar, and E. Thomas, "Correlation between body mass index and dental caries among three- to 12-year-old schoolchildren in India: a cross-sectional study," *Cureus*, vol. 11, article e5421, 2019.

[27] A. Goodarzi, A. Heidarnia, S. S. Tavafian, and M. Eslami, "Association between dental caries and body mass index-for-age among 10-12-year-old female students in Tehran," *International Journal of Preventive Medicine*, vol. 10, p. 28, 2019.

[28] J. J. Liang, Z. Q. Zhang, Y. J. Chen et al., "Dental caries is negatively correlated with body mass index among 7-9 years old children in Guangzhou," *China. BMC Public Health*, vol. 16, p. 638, 2016.

[29] P. Gupta, N. Gupta, and H. P. Singh, "Prevalence of dental caries in relation to body mass index, daily sugar intake, and oral hygiene status in 12-year-old school children in Mathura City: a pilot study," *International Journal Of Pediatrics*, vol. 2014, Article ID 921823, 2014.

[30] A. Elangovan, J. Mungara, and E. Joseph, "Exploring the relation between body mass index, diet, and dental caries among 6-12-year-old children," *Journal of the Indian Society of Pedodontics and Preventive Dentistry*, vol. 30, pp. 293–300, 2012.

[31] C. Norberg, U. Hallstrom Stalin, L. Matsson, K. Thorngren-Jerneck, and G. Klingberg, "Body mass index (BMI) and dental caries in 5-year-old children from southern Sweden," *Community Dentistry and Oral Epidemiology*, vol. 40, pp. 315–322, 2012.

[32] M. Sadeghi and F. Alizadeh, "Association between dental caries and body mass index-for-age among 6-11-year-old children in Isfahan in 2007," *J Dent Res Dent Clin Dent Prospects*, vol. 1, pp. 119–124, 2007.

[33] E. W. Gerdin, M. Angbratt, K. Aronsson, E. Eriksson, and I. Johansson, "Dental caries and body mass index by socioeconomic status in Swedish children," *Community Dentistry and Oral Epidemiology*, vol. 36, pp. 459–465, 2008.

[34] J. S. Choi, N. H. Park, S. Y. Hwang et al., "The antibacterial activity of various saturated and unsaturated fatty acids against several oral pathogens," *Journal of Environmental Biology*, vol. 34, no. 4, pp. 673–676, 2013.

[35] V. L. Murty, B. L. Slomiany, W. Laszewicz, A. Slomiany, K. Petropoulou, and I. D. Mandel, "Lipids of developing dental plaque in caries-resistant and caries-susceptible adult people," *Archives of Oral Biology*, vol. 30, pp. 171–175, 1985.

[36] A. Kensche, M. Reich, K. Kummerer, M. Hannig, and C. Hannig, "Lipids in preventive dentistry," *Clinical Oral Investigations*, vol. 17, pp. 669–685, 2013.

[37] S. Karjalainen, "Eating patterns, diet and dental caries," *Dental Update*, vol. 34, no. 5, pp. 295–300, 2007.

[38] S. H. Al Rawahi, K. Asimakopoulou, and J. T. Newton, "Theory based interventions for caries related sugar intake in adults: systematic review," *BMC Psychology*, vol. 5, p. 25, 2017.

[39] B. G. Bibby, "The cariogenicity of snack foods and confections," *The Journal of the American Dental Association*, vol. 90, no. 1, pp. 121–132, 1975.

[40] M. I. Pavlov and C. Naulin-Ifi, "Plea for prevention and early management of baby bottle tooth decay syndrome," *Archives de Pédiatrie*, vol. 6, pp. 218–222, 1999.

[41] S. Tungare and A. G. Paranjpe, *Baby Bottle Syndrome*, In StatPearls, Treasure Island (FL), 2020.

[42] A. Oklahorna Dental, "ODA patient's page Baby bottle syndrome," *Journal-Oklahoma Dental Association*, vol. 100, 2009.

[43] M. Muller-Giamarchi and J. R. Jasmin, "Baby-bottle syndrome," *Pédiatrie*, vol. 45, no. 7-8, pp. 485–489, 1990.

[44] J. Buchan, "The "bottle baby" syndrome," *International Nursing Review*, vol. 26, pp. 141–144, 1979.

[45] J. Khadra-Eid, D. Baudet, M. Fourny, E. Sellier, C. Brun, and P. François, "Development of a screening scale for children at risk of baby bottle tooth decay," *Archives de Pediatrie: Organe Officiel de la Societe Francaise de Pediatrie*, vol. 19, no. 3, pp. 235–241, 2012.

[46] A. Gutierrez Gossweiler and E. A. Martinez-Mier, "Chapter 6: vitamins and oral health," *Monographs in Oral Science*, vol. 28, pp. 59–67, 2020.

[47] B. Gora, "The effect of vitamin A deficiency on the oral epithelium in diet of white rats. II. Histochemical studies," *Czasopismo Stomatologiczne*, vol. 26, no. 10, pp. 1155–1162, 1973.

[48] B. Gora, "The effect of vitamin A deficiency in the diet of white rats on the epithelium of the oral mucosa. 1. Morphological studies," *Czasopismo Stomatologiczne*, vol. 26, no. 10, pp. 1145–1153, 1973.

[49] D. De Rasmo, G. Palmisano, S. Scacco et al., "Phosphorylation pattern of the NDUFS4 subunit of complex I of the mammalian respiratory chain," *Mitochondrion*, vol. 10, no. 5, pp. 464–471, 2010.

[50] A. Ujevic, L. Lugovic-Mihic, M. Situm, L. Ljubesic, J. Mihic, and N. Troskot, "Aphthous ulcers as a multifactorial problem," *Acta Clinica Croatica*, vol. 52, no. 2, pp. 213–221, 2013.

[51] H. L. Liu and S. C. Chiu, "The Effectiveness of Vitamin B12 for Relieving Pain in Aphthous Ulcers: A Randomized, Double-blind, Placebo-controlled Trial," *Pain Management Nursing*, vol. 16, no. 3, pp. 182–187, 2015.

[52] B. L. Weusten and A. van de Wiel, "Aphthous ulcers and vitamin B12 deficiency," *The Netherlands Journal of Medicine*, vol. 53, pp. 172–175, 1998.

[53] M. Carrozzo, M. Carbone, and S. Gandolfo, "Recurrent aphthous stomatitis: current etiopathogenetic and therapeutic concepts," *Minerva Stomatologica*, vol. 44, no. 10, pp. 467–475, 1995.

[54] D. Wray, M. M. Ferguson, D. K. Mason, A. W. Hutcheon, and J. H. Dagg, "Recurrent aphthae: treatment with vitamin B12, folic acid, and iron," *British Medical Journal*, vol. 2, pp. 490–493, 1975.

[55] M. F. La Via, D. R. Weathers, S. N. Kreitzman, C. E. Waldron, and G. Teti, "Relationship of vitamin A intake and E rosette inhibition to oral dysplasia and neoplasia," *Cancer Detection and Prevention*, vol. 4, no. 1-4, pp. 121–128, 1981.

[56] C. Scully and P. Boyle, "Vitamin A related compounds in the chemoprevention of potentially malignant oral lesions and carcinoma," *Part B, Oral oncology*, vol. 28, no. 2, pp. 87–89, 1992.

[57] D. Kuzmanova, I. D. Jansen, T. Schoenmaker et al., "Vitamin C in plasma and leucocytes in relation to periodontitis," *Journal of Clinical Periodontology*, vol. 39, pp. 905–912, 2012.

[58] X. Zhang, H. Meng, X. Sun et al., "Elevation of vitamin D-binding protein levels in the plasma of patients with generalized aggressive periodontitis," *Journal of Periodontal Research*, vol. 48, pp. 74–79, 2013.

[59] K. N. Liu, H. X. Meng, X. L. Tang et al., "Correlation analysis between plasma levels of 25-hydroxy vitamin D3 and osteocalcin in patients with aggressive periodontitis," *Beijing Da Xue Xue Bao Yi Xue Ban*, vol. 41, no. 1, pp. 49–51, 2009.

[60] A. T. Merchant, "Plasma vitamin C is inversely associated with periodontitis," *The Journal of Evidence-Based Dental Practice*, vol. 8, pp. 103-104, 2008.

[61] P. J. Pussinen, T. Laatikainen, G. Alfthan, S. Asikainen, and P. Jousilahti, "Periodontitis is associated with a low concentration of vitamin C in plasma," *Clinical and Diagnostic Laboratory Immunology*, vol. 10, pp. 897–902, 2003.

[62] A. Ballini, S. Scacco, M. Boccellino, L. Santacroce, and R. Arrigoni, "Microbiota and obesity: where are we now?," *Biology (Basel)*, vol. 9, no. 12, p. 415, 2020.

[63] T. Saito, Y. Shimazaki, and M. Sakamoto, "Obesity and periodontitis," *The New England Journal of Medicine*, vol. 339, pp. 482-483, 1998.

[64] N. N. Gulati, S. S. Masamatti, and P. Chopra, "Association between obesity and its determinants with chronic periodontitis: a cross-sectional study," *J Indian Soc Periodontol*, vol. 24, pp. 167–172, 2020.

[65] S. Arboleda, M. Vargas, S. Losada, and A. Pinto, "Review of obesity and periodontitis: an epidemiological view," *British Dental Journal*, vol. 227, pp. 235–239, 2019.

[66] E. P. Zuza, V. G. Garcia, L. H. Theodoro et al., "Influence of obesity on experimental periodontitis in rats: histopathological, histometric and immunohistochemical study," *Clinical Oral Investigations*, vol. 22, pp. 1197–1208, 2018.

[67] P. G. Moura-Grec, J. A. Marsicano, C. A. Carvalho, and S. H. Sales-Peres, "Obesity and periodontitis: systematic review and meta-analysis," *Ciência & Saúde Coletiva*, vol. 19, no. 6, pp. 1763–1772, 2014.

[68] H. J. Lee, J. K. Jun, S. M. Lee, J. E. Ha, D. I. Paik, and K. H. Bae, "Association between obesity and periodontitis in pregnant females," *Journal of Periodontology*, vol. 85, pp. e224–e231, 2014.

[69] C. Gocke, B. Holtfreter, P. Meisel et al., "Abdominal obesity modifies long-term associations between periodontitis and markers of systemic inflammation," *Atherosclerosis*, vol. 235, pp. 351–357, 2014.

[70] P. Bullon, H. N. Newman, and M. Battino, "Obesity, diabetes mellitus, atherosclerosis and chronic periodontitis: a shared pathology via oxidative stress and mitochondrial dysfunction?," *Periodontology 2000*, vol. 64, no. 1, pp. 139–153, 2014.

[71] F. Boesing, J. S. Patino, V. R. da Silva, and E. A. Moreira, "The interface between obesity and periodontitis with emphasis on oxidative stress and inflammatory response," *Obesity Reviews*, vol. 10, pp. 290–297, 2009.

[72] S. Enhos, I. Duran, S. Erdem, and S. Buyukbas, "Relationship between iron-deficiency anemia and periodontal status in female patients," *Journal of Periodontology*, vol. 80, no. 11, pp. 1750–1755, 2009.

[73] A. T. Merchant, W. Pitiphat, M. Franz, and K. J. Joshipura, "Whole-grain and fiber intakes and periodontitis risk in men," *The American Journal of Clinical Nutrition*, vol. 83, pp. 1395–1400, 2006.

[74] J. T. van der Tas, M. E. C. Elfrink, A. C. Heijboer et al., "Foetal, neonatal and child vitamin D status and enamel hypomineralization," *Community Dentistry and Oral Epidemiology*, vol. 46, pp. 343–351, 2018.

[75] J. Kühnisch, E. Thiering, R. Heinrich-Weltzien, E. Hellwig, R. Hickel, and J. Heinrich, "Fluoride/vitamin D tablet supplementation in infants-effects on dental health after 10 years," *Clinical Oral Investigations*, vol. 21, pp. 2283–2290, 2017.

[76] M. Dioguardi, C. Quarta, D. Sovereto et al., "Autotransplantation of the third molar: a therapeutic alternative to the rehabilitation of a missing tooth: a scoping review," *Bioengineering (Basel)*, vol. 8, no. 9, p. 120, 2021.

[77] D. Hallas, N. G. Herman, L. Benichou, E. L. Morales, and L. Touchette, "Management of a child with nutritional rickets, multiple cavities, enamel hypoplasia, and reactive attachment disorder," *Journal of pediatric health care: official publication of National Association of Pediatric Nurse Associates & Practitioners*, vol. 29, pp. 283–288, 2015.

[78] S. Hancock, C. Zinn, and G. Schofield, "The consumption of processed sugar- and starch-containing foods, and dental caries: a systematic review," *European Journal of Oral Sciences*, vol. 128, pp. 467–475, 2020.

[79] G. J. van der Putten, J. Vanobbergen, L. De Visschere, J. Schols, and C. de Baat, "Association of some specific nutrient deficiencies with periodontal disease in elderly people: a systematic literature review," *Nutrition*, vol. 25, pp. 717–722, 2009.

[80] U. Van der Velden, "Vitamin C and its role in periodontal diseases-the past and the present: a narrative review," *Oral Health & Preventive Dentistry*, vol. 18, pp. 115–124, 2020.

[81] S. Gaur and R. Agnihotri, "Trace mineral micronutrients and chronic periodontitis-a review," *Biological Trace Element Research*, vol. 176, pp. 225–238, 2017.

[82] H. Dommisch, D. Kuzmanova, D. Jönsson, M. Grant, and I. Chapple, "Effect of micronutrient malnutrition on

periodontal disease and periodontal therapy," *Periodontology 2000*, vol. 78, no. 1, pp. 129–153, 2018.

[83] T. López del Val, C. F. Estivariz, P. Martínez de Icaya, M. A. Jaunsolo, D. del Olmo, and V. Martínez, "Consumption of sweets and snacks by a population of school children in the Autonomous Community of Madrid. The CAENPE Group," *Medicina Clínica (Barcelona)*, vol. 109, pp. 88–91, 1997.

[84] M. Iwasaki, M. C. Manz, P. Moynihan et al., "Relationship between saturated fatty acids and periodontal disease," *Journal of Dental Research*, vol. 90, pp. 861–867, 2011.

[85] E. Macri, F. Lifshitz, C. Ramos et al., "Atherogenic cholesterol-rich diet and periodontal disease," *Archives of Oral Biology*, vol. 59, pp. 679–686, 2014.