

Article

Not peer-reviewed version

Survey Results of the Oral Hygiene Habits (Pre and Post Recommendations) among Phenylketonuria Patients in Latvia

[Iveta Abola](#)*, Nikola Anna Intlere, Anda Brinkmane, Sabine Laktina, Agnese Zarina, [Lauma Vasilevska](#), [Ingus Skadins](#), Georgijs Moisejevs, [Linda Gailite](#), [Madara Auzenbaha](#)

Posted Date: 8 December 2023

doi: 10.20944/preprints202312.0607.v1

Keywords: phenylketonuria; oral health; recommendations of daily oral hygiene procedures



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Article

Survey Results of the Oral Hygiene Habits (Pre and Post Recommendations) among Phenylketonuria Patients in Latvia

Iveta Abola ^{1,2,*}, Nikola Anna Intlere ¹, Anda Brinkmane ¹, Sabine Laktina ³, Agnese Zarina ^{3,4}, Lauma Vasilevska ³, Ingus Skadins ⁴, Georgijs Moisejevs ^{2,5}, Linda Gailite ² and Madara Auzenbaha ^{2,3,4}

¹ Department of Conservative Dentistry and Oral Health, Rīga Stradiņš University, LV-1007 Rīga, Latvia

² Scientific Laboratory of Molecular Genetics, Rīga Stradiņš University, LV-1007 Rīga, Latvia

³ Clinic of Medical Genetics and Prenatal Diagnostics, Children's Clinical University Hospital, LV-1004 Rīga, Latvia

⁴ Department of Biology and Microbiology, Rīga Stradiņš University, LV-1007 Rīga, Latvia

⁵ Jekabpils Regional Hospital, LV-5201, Jekabpils, Latvia

* Correspondence: abola.iveta@gmail.com

Abstract: Background: The aim of this study was to evaluate Phenylketonuria (PKU) patients' oral health habits and the efficiency of tailored recommendations for PKU patients in Latvia on the correct management of oral hygiene. The free amino acid formula can negatively impact PKU patient's oral health as it contains a high amount of complex carbohydrates. **Materials and methods:** In this study with a one-month interval pre and post implementation of oral hygiene recommendations, two questionnaires regarding oral hygiene habits and knowledge were prepared and provided by trained medical personnel to be filled in for all diagnosed PKU patients in Latvia who were not lost to follow-up. **Results:** Based on the questionnaires among the PKU patients under 18 years of age, 27% cleaned their teeth once a day. However, 6% of patients did not engage in regular teeth brushing at all. Among PKU patients over and 18 years of age, 26% brushed their teeth only once a day. Additionally, a mere 39% of PKU patients ≥ 18 years of age and 17% < 18 years of age incorporated flossing into their oral hygiene routine. In total, 45% of PKU patients ≥ 18 years of age and 44% < 18 years of age visited a dentist once a year, but 40% ≥ 18 years of age and 39% < 18 years of age visited a dentist less often than once per year. After reading the recommendations, a remarkable number of PKU patients < 18 years of age had improved their daily oral hygiene routine, including toothbrushing (25%) and flossing (23%). **Conclusion:** Given the unique dietary requirements and the implementation of these daily at-home oral health practices, motivation and regular reminders should result in better oral health of PKU patients and cooperation with clinicians.

Keywords: phenylketonuria; oral health; recommendations of daily oral hygiene procedures

1. Introduction

Phenylketonuria (PKU) is a hereditary disorder of the metabolism, with an autosomal recessive pattern of inheritance [1].

PKU treatment mainly consists of lowering proteins in the diet to ensure that phenylalanine (Phe) does not accumulate and have a toxic impact [2]. Patients diagnosed with classic PKU present with strict dietary requirements, allowing for a restricted intake of approximately 5–6 g of natural proteins per day. Furthermore, the ingestion of artificial sweeteners, such as aspartame and its derivatives, is not allowed due to their Phe composition [3].

To ensure appropriate growth and caloric intake, individuals with PKU rely on specialized amino acid mixtures as substitutes for natural proteins [4].

PKU patients need to be recommended to rinse their mouth with water immediately after consuming the PKU formula to counteract the acidity in their oral cavity [5]. An increased acidity in the oral cavity too often or for prolonged periods of time results in the demineralisation of tooth

structures. This process is known as dental caries, and all PKU patients are susceptible to higher levels of caries activity due to their dietary needs [6].

Oral health is an essential part of general health, and maintaining good oral hygiene is vital to sound general health [7]. The two most common oral diseases are dental caries and periodontal diseases, and plaque causes these common oral diseases [8]. Elimination of plaque is essential in the maintenance of good oral hygiene and hence good oral health. Brushing teeth twice a day with fluoridated toothpaste and flossing in between the teeth can help reduce plaque accumulation [9]. The daily oral procedure should also include a mouthwash to reduce the amount of plaque [10,11]. Also, regular dental check-up and professional dental hygiene procedure improves oral health [12].

Periodontitis, a chronic multifactorial inflammation of the periodontal tissue, is primarily caused by the accumulation of plaque and calculus on the teeth, leading to gum irritation and subsequent inflammation. This inflammatory process results in the development of gingivitis, an early reversible form of periodontitis [13]. By consistently practising good oral hygiene, patients can effectively manage and reverse gingivitis, preventing this progression to more severe forms of periodontitis [14].

In most cases, incorrect and/or irregular teeth cleaning and lack of oral health form the direct cause of periodontal illness manifestations [15,16].

Consequently, based on objective findings from our recent study about the dental status and periodontal health of PKU patients in Latvia, overall, all PKU patients had a higher prevalence of carious teeth than controls, and the values of the oral hygiene indices were significantly higher [5], [6,17].

Hence, it was deemed necessary to develop tailored oral health recommendations for PKU patients in Latvia in the national language, with the aim of enhancing the oral health outcomes and reducing the risk of dental caries and periodontal disease.

The recommendations of daily oral hygiene procedures should include teeth brushing twice a day, flossing in between the teeth, tongue cleaning, and mouthwash as important aspects of maintaining the good oral health of PKU patients.

The aim of the study was to analyse the existing habits and oral hygiene knowledge through a questionnaire examining actions PKU patients take and tools they use in their daily oral hygiene routines before and after receiving tailored recommendations, to evaluate whether PKU patients practically implemented these recommendations in their daily hygiene routine.

2. Material and Methods

2.1. Ethics Approval

The present study obtained research approval from the Central Medical Ethics Committee prior to data collection under permission (no. 1/10-03-26). The study was conducted according to the Helsinki Declaration.

2.2. Survey

This study has been designed to meet STROBE guidelines.

In total, 48 PKU patients < 18 years of age and 31 PKU patients ≥18 years of age (mean age 30.37±7.96 years, 12 males) were included in this cross-sectional study in period 2022-2023. In total 79 patients—87% of all the living diagnosed PKU patients, excluding those lost to follow-up in Latvia. The study was performed by trained medical personnel who disseminated a questionnaire interviewing on the phone (Supplementary S1). The structured survey written in Latvian language, was completed, and sent to the expert for necessary feedback on the content, sensitivity, and standard settings. The survey included questions concerning the oral hygiene procedures, usage of toothpaste without aspartame, and mouth rinsing each time after intake of specialized amino acid mixtures. The questionnaire began with a brief explanation of the study's purposes and asked respondents to answer as sincerely as possible. The questionnaire was subjected to a pilot group of 15 PKU patients for its validation; modifications were made necessary to resolve ambiguities. All questions had the possibility to give only one possible answer. For patients < 18 years of age, questionnaires were filled

out by their parents. PKU patients received written recommendations comprising a set of 12 everyday tasks aimed at enhancing the understanding of oral health and preventing the rise of Phe levels, which can have adverse effects on the neurological wellbeing of patients (Supplementary S2). Recommendations were created by dentist and rare disease specialist. After one-month period each participant was contacted by phone call and repeated survey was conducted. In the group ≥ 18 three patients could not be contacted again.

Table 1. Daily oral hygiene habits in the study group before and after received tailored recommendations.

		Patients Younger than 18 years of age					* <i>p</i> -Value	Patients Older and 18 years of age					* <i>p</i> -Value
		Before Recommendations		After Recommendations				Before Recommendations		After Recommendations			
		n = 48	%	n = 48	%	Improvement %		n = 31	%	n = 28	%	Improvement %	
How often do you brush your teeth?	Once a day	13	27	4	8	-19	0.007	8	26	5	18	-8	0.539
	Twice a day	32	66	44	92	25		23	74	23	82	8	
	Less than daily	3	6	0	0	-6		0	0	0	0	0	
Do you use dental floss daily?	Yes	8	17	19	40	23	0.023	12	39	9	32	-7	0.799
	No	40	83	29	60	-23		19	61	19	68	7	
How often do you visit a dentist?	Twice a year	7	15	20	42	27	<0.001	5	16	8	29	12	0.498
	Once a year	21	44	27	56	12		14	45	10	36	-9	
	Rarely	19	40	1	2.	-37		12	39	10	36	-3	
How often do you go to a dental hygienist?	Twice a year	8	17	16	33	17	<0.001	4	13	8	29	16	0.289
	Once a year	17	35	26	54	19		10	32	6	21	-11	
	Rarely	23	48	6	12	-35		17	55	14	50	-5	
Do you consistently rinse your mouth with water after each use of an amino acid-based formula?	Yes	9	19	13	27	8.	0.364	13	42	9	32	-10	0.284
	No	18	37	12	25	-12		15	48	12	43	-5	
	Drink water or use other methods	21	44	23	48	4.			3	10	7	25	
* Chi-square test													

2.3. Statistical Analysis

Statistical analysis was conducted using SPSS for Windows (SPSS, version R 4.1.2, SPSS Inc., Chicago, IL, USA). A p -value of <0.05 was considered as an indicator of a statistically significant result calculated by Chi-square Test.

3. Results

In Table 1 showed questionnaire results it does not reflect all the questions gathered from survey, only those that could be clarified in the necessary time interval. SurveBased on the questionnaires from the PKU patients < 18 years of age, 66% acknowledged brushing their teeth twice a day, while 27% cleaned their teeth once a day. However, alarmingly, 6% of patients did not engage in regular teeth brushing at all ($p=0.007$). Among PKU patients ≥ 18 years of age, 74% brushed their teeth twice a day, while 26% brushed only once a day ($p=0.539$). Additionally, a mere 39% of PKU patients ≥ 18 years of age and 17% < 18 years of age incorporated flossing into their daily oral hygiene routine, with the majority (61% and 83%) neglecting any form of interdental cleaning methods.

For PKU patients, it is recommended to use mouthwash on a daily basis to help to reduce dental plaque. The results show that 85% PKU patients < 18 years of age and 55% PKU patients ≥ 18 years of age do not use mouthwash at all.

According to questionnaires, 87% of PKU patients < 18 years of age and 42% ≥ 18 years of age use toothpaste without aspartame. There are patients who do not have enough knowledge which toothpastes to use, and a large number of these patients do not have clarity about aspartame (48% < 18 years of age); but one month after the recommendations and reminders of aspartame, the survey results were different in the group < 18 years of age ~80% were using toothpaste without aspartame, and in the group ≥ 18 years of age, it was 60%. An improvement of 20% was seen in group \geq than 18 years.

In the questionnaires, only 16% of PKU patients ≥ 18 years of age ($p=0.489$) and 15% < 18 years of age visit the dentist twice a year ($p<0.001$), 45% and 44% visit once a year, but 39% ≥ 18 years of age and 40% < 18 years of age visit the dentist less often than once a year.

Table 1 shows the frequency of visits to the dental hygienist as well before and after given recommendations.

It is important to mention that 90% of patients from both of groups agree that the provided recommendations will improve their daily oral procedures.

One month after receiving the recommendations (Supplementary S2), the survey was repeated. The largest changes were found in the group < 18 years of age, which indicates that the parents of PKU patients read them and hopefully will try to comply. However, 52% of those < 18 years of age and 43% ≥ 18 years of age claimed that given the recommendations positively influenced the oral hygiene outcomes, which was confirmed by further targeted questions.

For instance, before the given recommendations, 66% of PKU patients < 18 years of age were brushing their teeth twice a day comparing to 92% after ($p=0.007$). In addition, 40% of PKU patients < 18 years of age started flossing their teeth daily compared with 17% before ($p = 0.023$).

Further, 42% of PKU patients < 18 years of age plan to schedule a visit to the dentist twice a year, while before the recommendations, it was 15% ($p < 0.001$). The same result was seen in terms of visits to the hygienist, increasing from 17% to 33% ($p < 0.001$).

In the survey for the group >18 years were included question about their current education - 20% of adult PKU patients have higher education and 23% needed special education, the rest has general secondary or vocational secondary education.

4. Discussion

The present study aimed to investigate oral hygiene habits behaviour among PKU patients in Latvia.

Dental caries (tooth decay) and periodontal diseases (gingivitis and periodontitis) affect most people worldwide, causing pain, eating, and speaking difficulties, low self-esteem, tooth loss and the

need for surgery. As dental plaque is the primary cause for dental caries and periodontal disease, daily oral hygiene procedures and removal of plaque is important for oral health [18].

Toothbrushing is considered fundamental self-care behaviour for the maintenance of oral health, and brushing twice a day has become a social norm [19]. The fact that only 74% of PKU patients ≥ 18 years of age and 67% < 18 years of age brush their teeth twice a day is a proof that oral hygiene knowledge and motivation remain low for PKU patients in Latvia.

Upon examination of the dental status and periodontal health examination of PKU patients in Latvia, a notable observation surfaced, revealing that an overwhelming majority (93%) need professional dental cleaning performed by a dental hygienist [5].

Using floss or interdental brushes in addition to toothbrushing is also very important to remove plaque between two adjacent teeth. It may reduce gingivitis more than toothbrushing alone [20]. It is strongly recommended to use daily interdental cleaning devices and mouthwash, in addition to toothbrushing, for preventing and controlling periodontal diseases and dental caries [21].

According to our questionnaire, only 39% of PKU patients ≥ 18 years of age and 17% of PKU patients < 18 years of age use dental floss daily. It makes one wonder about parents' knowledge, role, and modelling of daily hygiene procedures as well as the dental practitioner's constant reminders of proper oral health daily care. It should be noted again that after being given recommendations, the number of PKU patients who floss their teeth increased.

A daily mouthwash is recommended for PKU patients to reduce dental plaque. The survey results show that 15% of PKU patients < 18 years of age and 45% of PKU patients ≥ 18 years of age use mouthwash on daily basis. From these results, we conclude that there are still a large number of patients that can be introduced to natural formulation mouthwashes, as more than 80% of PKU patients have not heard about them or did not include them in their daily hygiene procedures.

Neves et al. in their study demonstrated the crucial role of the family on the oral health of their children [22]. The priorities of parents of children with PKU lie more in maintaining an optimal general health and daily functioning of the child rather than focusing on prevention of oral disease. Children with chronic medical conditions and their families have many pressures placed upon them, and there is often a delay in seeking dental care as it is simply not a priority [23].

Another important variable that determines the overall wellbeing of PKU patients, including their oral health, is the level of education of the parents. It has been reported that the higher the education level of the parents, the greater the understanding of the disease, and the greater the support for the affected child [24]. Tadakamadla et al. investigated that adolescents' oral health habits are reported to be closely related to parents' educational background, family structure, and income and that children's and parents' toothbrushing habits have significant similarities [25]. As for adults with PKU, it has been proposed that the increased risk of oral health issues may be due to social burdens [17,26]. Important to mention, when interviewing PKU patients, the level of education was ascertained only for adult patients, but not for parents of younger ones. 20% of adult PKU patients have higher and 23% special education. Patients with higher education level more likely practice oral hygiene, brushing teeth more often and having regular dental checkups [27].

Through consultations and patient interviews, a noteworthy observation emerged, indicating that individuals with PKU not only exhibit poor oral health compared to the control group. Patients reported limited awareness among dentists and dental hygienists about the specific challenges associated with phenylketonuria and its impact on oral health and hygiene.

Patients with PKU must carefully select their toothpastes by taking into consideration their formulation. It is important that the toothpaste contains fluorides while avoiding the inclusion of aspartame, a sweetener. Survey results show that 87% of PKU patients < 18 years of age and 42% ≥ 18 years of age claim that the toothpaste they are using does not contain aspartame. When the dentist asks the name of the toothpaste, the answers show the opposite—these toothpastes do contain aspartame. Unfortunately, this leads to the conclusion that PKU patients and their parents do not pay attention to such important details, and probably in recommendations, they should be given more information about it.

In the recommendations (Supplement 2) were included information about saliva stimulation. Saliva is an important factor in a plethora of oral functions, such as mastication, swallowing, antimicrobial activity, and cleaning action [28]. The investigation into the oral health of PKU patients in Latvia revealed that 60% of PKU patients had a decreased basal saliva secretion rate compared with healthy counterparts [5]. Saliva influences oral health both through its nonspecific physiochemical properties, as well as through more specific effects [28]. Salivation can be induced by gustatory or masticatory stimulation, such as using a chewing gum [29]. Other desirable properties of chewing gums are an adequate buffer capacity and the use of non-cariogenic sweeteners such as xylitol, sorbitol, and mannitol. These sweeteners will not result in an increase in caries incidence due to the fermentation by oral microorganisms but will instead decrease the caries activity [30,31]. PKU patients and their parents should know that chewing gum must not contain aspartame.

It is important to note that a considerable number of PKU patients have no knowledge about proper oral care procedures, as well as the fact that their toothpaste and chewing gum must not contain aspartame.

More attention should be provided to PKU patients' oral health. Dental and dental hygienist visits for caries prevention and gingival health were low, 39% PKU patients ≥ 18 years of age and 40% < 18 years of age visit the dentist less than once a year. Similarly, 55% of PKU patients ≥ 18 years of age and 48% < 18 years of age visit the dental hygienist less than once a year.

In the literature, the most recommended revisiting period for dental care is 6 months [32]. Dental professionals are convinced that frequent examinations allow disease to be detected and treated in time and preventive interventions to be delivered [33]. A clinical guideline recommends that the longest period between examinations for both children and adults should be 12 months; for adults maintaining good oral health and appropriate home care habits, this may be extended to 24 months [33,34].

The investigation of dental status and periodontal health among PKU patients, showed a notable finding indicating that PKU patients exhibit statistically poorer dental and periodontal health compared with healthy individuals, including a higher prevalence of dental caries and elevated hygiene index rates (Silness-Löe, CPITN, Greene-Vermillion) [5], which implies poor oral health. This clearly shows the necessity of recommendations about oral daily hygiene procedures for every PKU patient.

Considering the survey results one month after the patients received the recommendations, the number of PKU patients who brushed their teeth twice a day increased, which could mean that there is a need to regularly remind patients to maintain oral health.

It is highly important that the metabolic team, dentists, general practitioners, and psychologists encourage, motivate, and support PKU patients to follow the recommendations of oral hygiene procedures, as 90% of PKU patients < 18 years of age and ≥ 18 years of age do believe that this will improve their oral health and sequentially overall quality of life. To increase the awareness among health care professionals to oral hygiene habits in PKU patients, there were published in local journal (*Latvijas Arsts*, August, 2023 <https://is.arstubi.driba.lv/magazine>).

The prophylactic prevention of dental caries and periodontal disease manifestations depend on the combination of diligent oral hygiene practices at home and regular visits to the dentist and dental hygienist. Patients who adhere to a regular routine schedule of dental check-ups demonstrate increased motivation to prioritize their oral health and maintain proper hygiene habits.

After questioning PKU patients and their parents, it becomes evident that the primary focus lies on monitoring the Phe levels and ensuring regular consumption of the prescribed amino acid mixture. Consequently, the adequate attention and care towards oral health often take a backseat, despite their crucial significance. This oversight is particularly critical when oral hygiene practices are not diligently followed, including the essential step of proper rinsing with water.

The limitation of the study should certainly be mentioned the small number of patients, but should admit, that it includes in total 79 patients, which is 87% of all the living diagnosed PKU patients in Latvia. It would be valuable to repeat the survey after the time to see long-term effect of recommendations.

5. Conclusions

Despite the small number of patients, the present study produced some significant finding on oral hygiene behaviour. PKU patients were found to have limited dental and dental hygienist visits, as well as insufficient caries prevention and professional teeth cleaning. Summarizing the results from the questionnaires, it was obvious that PKU patients must improve their oral health routines, such as their teeth brushing habits, the use of interdental cleaning tools, and mouthwash.

We conclude that there is a need to regularly remind patients to maintain oral health, for example, through annual questionnaires that provide daily oral hygiene recommendations. The reminders could be included in annual PKU patient's visits to a dietitian and geneticist.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

Author Contributions: Conceptualization, investigation, data collecting, writing – original draft preparation – Iveta Abola; methodology – Madara Auzenbaha, Linda Gailite; validation – Ingus Skadins; investigation - Anda Brinkmane, Georgijs Moisejevs; data curation – Nikola Anna Intlere; data collecting - Sabine Laktina, Agnese Zarina, Lauma Vasilevska; writing – review and editing – Madara Auzenbaha; project administration – Linda Gailite. All authors have read and agreed to the published version of manuscript.

Funding: No external funding.

Institutional Review Board Statement: The present study obtained research approval from the Central Medical Ethics Committee prior to data collection under permission (nr. 1/10-03-26). The study was conducted according to the Helsinki Declaration.

Informed Consent Statement: All participants and their parents provided informed written consent.

Data Availability Statement: Data Availability Statements are available in section "MDPI Research Data Policies" at <https://www.mdpi.com/ethics>.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. R. Lugovska, P. Vevere, R. Andrusaite, and A. Kornejeva, "Newborn screening for PKU and congenital hypothyroidism in Latvia," *Southeast Asian J. Trop. Med. Public Health*, 1999.
2. A. M. J. van Wegberg *et al.*, "The complete European guidelines on phenylketonuria: diagnosis and treatment," *Orphanet J. Rare Dis.*, vol. 12, no. 1, p. 162, Oct. 2017, doi: 10.1186/s13023-017-0685-2.
3. V. Maler *et al.*, "Aspartame and Phenylketonuria: an analysis of the daily phenylalanine intake of aspartame-containing drugs marketed in France," *Orphanet J. Rare Dis.*, 2023, doi: 10.1186/s13023-023-02770-x.
4. N. A. Elhawary *et al.*, "Genetic etiology and clinical challenges of phenylketonuria," *Human Genomics*, 2022, doi: 10.1186/s40246-022-00398-9.
5. I. Abola, D. E. Emulina, I. Skadins, A. Brinkmane, L. Gailite, and M. Auzenbaha, "Dental Status and Periodontal Health of Patients with Phenylketonuria in Latvia," *Acta Stomatol. Croat.*, 2022, doi: 10.15644/asc56/2/2.
6. E. Ballikaya *et al.*, "Oral health status of children with phenylketonuria," *J. Pediatr. Endocrinol. Metab.*, 2020, doi: 10.1515/jpem-2019-0439.
7. S. A. H. Bokhari and A. A. Khan, "Growing burden of noncommunicable diseases: The contributory role of oral diseases, Eastern Mediterranean Region perspective," *Eastern Mediterranean Health Journal*, 2009, doi: 10.26719/2009.15.4.1011.
8. M. Sanz *et al.*, "Role of microbial biofilms in the maintenance of oral health and in the development of dental caries and periodontal diseases. Consensus report of group 1 of the Joint EFP/ORCA workshop on the boundaries between caries and periodontal disease," *J. Clin. Periodontol.*, 2017, doi: 10.1111/jcpe.12682.
9. L. Rimondini, B. Zolfanelli, F. Bernardi, and C. Bez, "Self-preventive oral behavior in an Italian university student population," *J. Clin. Periodontol.*, 2001, doi: 10.1034/j.1600-051x.2001.028003207.x.
10. C. Erbe, M. Klukowska, H. C. Timm, M. L. Barker, J. Van Der Wielen, and H. Wehrbein, "A randomized controlled trial of a power brush/irrigator/mouthrinse routine on plaque and gingivitis reduction in orthodontic patients," *Angle Orthod.*, 2019, doi: 10.2319/022618-159.1.
11. P. G. Arduino *et al.*, "Effect of two different alcohol-free chlorhexidine formulations in mouthrinses on the immediate postoperative period for oral mucosal biopsies," *J. Oral Sci.*, 2020, doi: 10.2334/josnusd.19-0225.

12. S. Zheng, L. Zhao, N. Ju, T. Hua, S. Zhang, and S. Liao, "Relationship between oral health-related knowledge, attitudes, practice, self-rated oral health and oral health-related quality of life among Chinese college students: a structural equation modeling approach," *BMC Oral Health*, 2021, doi: 10.1186/s12903-021-01419-0.
13. N. Yu and T. E. Van Dyke, "Periodontitis: a Host-Mediated Disruption of Microbial Homeostasis," *Current Oral Health Reports*. 2020, doi: 10.1007/s40496-020-00256-4.
14. Color Atlas of Dental Hygiene: Periodontology. 2014.
15. J. S. Ericsson, K. H. Abrahamsson, A. L. Östberg, M. K. Hellström, K. Jönsson, and J. L. Wennström, "Periodontal health status in Swedish adolescents: An epidemiological, cross-sectional study," *Swed. Dent. J.*, 2009.
16. L. Musić, M. Par, J. Peručić, A. Badovinac, D. Plančak, and I. Puhar, "Relationship between halitosis and periodontitis: A pilot study," *Acta Stomatol. Croat.*, 2021, doi: 10.15644/ASC55/2/9.
17. A. C. Bingöl *et al.*, "Dietary and metabolic effects on the oral status of patients with phenylketonuria: a nation-based cross-sectional study," *Clin. Oral Investig.*, 2023, doi: 10.1007/s00784-022-04827-w.
18. S. Ebrahimipour, S. Bijari, F. Talebi, and S. Darmiani, "THE EFFECT OF ORAL HEALTH EDUCATION ON DENTAL PLAQUE AND GINGIVAL INDEX OF FEMALE STUDENTS BY THE VIRTUAL REALITY SIMULATION METHOD," *Int. J. Med. Dent.*, 2022.
19. S. Kumar, J. Tadakamadla, and N. W. Johnson, "Effect of toothbrushing frequency on incidence and increment of dental caries: A systematic review and meta-analysis," *Journal of Dental Research*. 2016, doi: 10.1177/0022034516655315.
20. E. B. Fleming, D. Nguyen, J. Afful, M. D. Carroll, and P. D. Woods, "Prevalence of daily flossing among adults by selected risk factors for periodontal disease—United States, 2011–2014," *J. Periodontol.*, 2018, doi: 10.1002/JPER.17-0572.
21. H. V. Worthington *et al.*, "Home use of interdental cleaning devices, in addition to toothbrushing, for preventing and controlling periodontal diseases and dental caries," *Cochrane Database of Systematic Reviews*. 2019, doi: 10.1002/14651858.CD012018.pub2.
22. É. T. B. Neves *et al.*, "The impact of oral health literacy and family cohesion on dental caries in early adolescence," *Community Dent. Oral Epidemiol.*, 2020, doi: 10.1111/cdoe.12520.
23. A. M. Moursi, J. B. Fernandez, M. Daronch, L. Zee, and C. L. Jones, "Nutrition and oral health considerations in children with special health care needs: Implications for oral health care providers," *Pediatr. Dent.*, 2010.
24. I. P. S. Castro, J. M. Borges, H. A. Chagas, J. Tibúrcio, A. L. P. Starling, and M. J. B. De Aguiar, "Relationships between phenylalanine levels, intelligence and socioeconomic status of patients with phenylketonuria," *J. Pediatr. (Rio. J.)*, 2012, doi: 10.2223/JPED.2175.
25. S. K. Tadakamadla, J. Tadakamadla, J. Kroon, R. Lalloo, and N. W. Johnson, "Effect of family characteristics on periodontal diseases in children and adolescents—A systematic review," *International Journal of Dental Hygiene*. 2020, doi: 10.1111/idh.12398.
26. C. Cazzorla *et al.*, "Living with phenylketonuria in adulthood: The PKU ATTITUDE study," *Mol. Genet. Metab. Reports*, 2018, doi: 10.1016/j.ymgmr.2018.06.007.
27. G. Minervini, R. Franco, M. M. Marrapodi, L. Fiorillo, G. Cervino, and M. Cicciù, "The association between parent education level, oral health, and oral-related sleep disturbance. An observational crosssectional study," *Eur. J. Paediatr. Dent.*, 2023, doi: 10.23804/ejpd.2023.1910.
28. M. W. J. Dodds, D. A. Johnson, and C. K. Yeh, "Health benefits of saliva: A review," *J. Dent.*, 2005, doi: 10.1016/j.jdent.2004.10.009.
29. H. Olsson, C. J. Spak, and T. Axéll, "The effect of a chewing gum on salivary secretion, oral mucosal friction, and the feeling of dry mouth in xerostomic patients," *Acta Odontol. Scand.*, 1991, doi: 10.3109/00016359109005919.
30. D. Kandelman and G. Gagnon, "Clinical Results After 12 Months from a Study of the Incidence and Progression of Dental Caries in Relation to Consumption of Chewing-gum Containing Xylitol in School Preventive Programs," *J. Dent. Res.*, 1987, doi: 10.1177/00220345870660082501.
31. S. Kashket, T. Yaskell, and L. R. Lopez, "Prevention of Sucrose-induced Demineralization of Tooth Enamel by Chewing Sorbitol Gum," *J. Dent. Res.*, 1989, doi: 10.1177/00220345890680030401.
32. P. A. Fee, P. Riley, H. V. Worthington, J. E. Clarkson, D. Boyers, and P. V. Beirne, "Recall intervals for oral health in primary care patients: a Cochrane review," *Dent. Cadmos*, 2022, doi: 10.19256/d.cadmos.01.2022.05.
33. National Institute for Clinical Excellence, "Dental recall Recall interval between routine dental examinations," *Nice*, 2004.
34. N. J. Wang, C. Källestål, P. E. Petersen, and I. B. Arnadottir, "Caries preventive services for children and adolescents in Denmark, Iceland, Norway and Sweden: Strategies and resource allocation," *Community Dent. Oral Epidemiol.*, 1998, doi: 10.1111/j.1600-0528.1998.tb01960.x.

35. N. C. Krupa, H. M. Thippeswamy, and B. R. Chandrashekar, "Antimicrobial efficacy of Xylitol, Probiotic and Chlorhexidine mouth rinses among children and elderly population at high risk for dental caries - A Randomized Controlled Trial," *J. Prev. Med. Hyg.*, 2022, doi: 10.15167/2421-4248/jpmh2022.63.2.1772.
36. M. Siddharth, P. Singh, R. Gupta, A. Sinha, S. Shree, and K. Sharma, "Comparative Evaluation of Subgingivally Delivered 2% Curcumin and 0.2% Chlorhexidine Gel Adjunctive to Scaling and Root Planing in Chronic Periodontitis," *J. Contemp. Dent. Pract.*, 2020, doi: 10.5005/JIP-JOURNALS-10024-2828.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.