Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/medici

Original Research Article

Do hemophiliacs have a higher risk for dental caries than the general population?

Rūta Žaliūnienė[a,*], *Jolanta Aleksejūnienė*[b], *Vilma Brukienė*[a], *Vytautė Pečiulienė*[a]

[a] *Institute of Dentistry, Medical Faculty, Vilnius University, Vilnius, Lithuania*
[b] *Faculty of Dentistry, University of British Columbia, Vancouver, Canada*

ARTICLE INFO

Article history:
Received 9 April 2014
Accepted 6 January 2015
Available online 28 January 2015

Keywords:
Dental caries
Dental public health
Hemophiliacs
Dental indices
Matched controls

ABSTRACT

Objective: The aim of this study was to examine if patients with hemophilia were at increased risk for dental decay as compared to the general population.

Materials and methods: Census sampling was used in this case–control study to recruit cases (patients with hemophilia) and a control group individuals recruited randomly from the general population, which were matched with cases based on gender, age and place of residence. Clinical examinations included dental health and salivary assessments (flow rate, buffer capacity, caries-associated bacteria) and a structured questionnaire which inquired about socioeconomic status and dental health-related behaviors.

Results: In the deciduous dentition, the overall caries experience (dmf) differed statistically significantly ($P = 0.003$) between the hemophiliacs (2.6 ± 2.6) and their matched healthy controls (6.1 ± 2.5). Bivariate analyses did not reveal significant differences between cases and controls regarding salivary functions, except that higher bacteriological counts were found in healthy controls in deciduous dentitions than in patients with hemophilia ($P = 0.019$). Children without hemophilia were from higher socioeconomic status families than hemophiliacs ($P = 0.004$), but such differences were not found for adults ($P = 0.090$). When compared to healthy adults, adult hemophiliacs had more gum bleeding at rest ($P < 0.001$) as well as during their tooth brushing ($P = 0.007$) and they also consumed more soft drinks than controls ($P = 0.025$).

Conclusions: Better dental health was observed in children with hemophilia as compared to children without it. There were no differences in dental health between adult hemophiliacs and healthy controls from the general population. None of the linear multiple regression models confirmed hemophilia to be an additional caries risk when it was controlled for other caries determinants.

* *Corresponding author at*: Institute of Dentistry, Medical Faculty, Vilnius University, Žalgirio 117, 08217 Vilnius, Lithuania.
E-mail address: zaliuniene@gmail.com (R. Žaliūnienė).

Peer review under responsibility of Lithuanian University of Health Sciences.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.medici.2015.01.003

1. Introduction

Dental treatments in hemophilia patients are challenging and have inherent health risks that can be life-threatening [1]. Hemophilia is a rare disease linked to males characterized by a defective blood clotting [2] with hemophilia A being the most common type with a prevalence of approximately one per 5000 male births and hemophilia B more rare with a prevalence of approximately one per 50,000 male births [3]. The mild form of either hemophilia A or B may be left undiagnosed until adolescence or even later in life, particularly if a patient did not have surgery, extensive dental work or serious trauma at an earlier age [4]. Given that up to 30% of mild hemophilia cases are first diagnosed following an episode of severe oral bleeding, it is important to increase awareness among dental professionals [5]. Congenital hemorrhagic disorders comprise only a small proportion of general diseases seen in any given population, and possibly this is why there are only a few studies concerning hemophilia and dental disease [6].

A higher severity of overall caries experience was reported among young hemophiliacs who had the severe type of either hemophilia A or B [7]. A higher caries experience in both patients with hemophilia or patients without it is associated with lifestyle factors such as inadequate oral self-care (presence of dental plaque) and sugar-containing diet as well as reduced host resistance. Thus, it is important to know whether patients with hemophilia as compared to the general population are at additional risk for dental decay when controlled for known caries-related determinants. A number of caries-related determinants are well established. Lower socioeconomic status (SES) has been associated with high caries rates in both children and adults [8–10] and explained by a detrimental oral health-related lifestyle such as frequent consumption of sugar-containing foods or drinks, lack of oral hygiene, infrequent dental visits or seeking dental care only when experiencing pain or some kind of problem observed in lower SES groups [11–13]. The frequent consumption of sugar-containing products and deficient oral hygiene are two main etiological factors associated with dental caries [14–16]. Sugar-containing diet and excessive drinking of juices are detrimental to dental health because these increase the acidity of saliva [17]. A deficiency of oral hygiene has also been associated with higher rates of dental decay [18]. Varying results concerning the oral hygiene of hemophiliacs have been reported. A study of Polish children demonstrated that oral hygiene was worse in hemophiliac children than in healthy children [6], while a study by Ziebolz et al. found the reverse was true for adults [19]. Another study focusing on the oral hygiene of children with severe hemophilia found that they had significantly better oral hygiene than healthy children [20]. Proper oral self-care contributes to lower levels of two tooth decay causing bacteria: *Streptococcus mutans* and *Lactobacilli* [21]. Unsurprisingly, the salivary levels of these bacteria were lower in children with hemophilia who had better oral hygiene than healthy controls [20]. The reason why some patients with hemophilia may avoid tooth brushing particularly when they notice gum bleeding [22] is that for some hemophiliacs even minor trauma such as tooth brushing, trauma from eating or infection can cause gingival bleeding [23].

To maintain healthy teeth, saliva is of major importance [24] with saliva buffer capacity and flow rate playing key protective roles against dental caries [25–27]. Saliva buffers acid attacks by resisting drop in pH in the saliva and by also allowing calcium ions to be released from the saliva, which contribute to the remineralization of tooth minerals [17]. On tooth surfaces there is a continuous interchange between the demineralization (loss of hard tooth tissue) resulting from diet and microbial activity and remineralization (repair of hard tissues) from the host defense. When this balance is disrupted, dental caries develop.

Most importantly, in Lithuania general dentists tend not to treat patients with hemophilia due to potential complications. As there are only a few oral pathologists and their offices are located in big cities, access to primary dental care for hemophiliacs is limited. Given these barriers to accessing primary care in Lithuania, we may expect that patients with hemophilia may have higher levels of dental diseases.

The aim of the present study was to examine if hemophilia patients have a higher risk to dental caries than general population.

2. Materials and methods

The study was approved by the Research Ethics Committee, Faculty of Medicine, Vilnius University. The present study included a group of cases (hemophilia patients) and a group of controls. Census sampling (all included) was used for recruiting cases, which were patients 4 years or older listed in a register of hemophilia patients ($N = 76$). The control group ($N = 79$) was chosen from the general population by randomly selecting subjects and matching them with cases based on gender, age and place of residence. To match for gender, only male controls were chosen and to match for age and residence, only males from the specific age groups were randomly selected from five administrative regions of Lithuania. The data for both study groups were collected from November 2011 to March 2013. The present study included a total of 76 registered hemophilia patients (census sampling), of which 27 were children and 49 were adults. The group of matched controls (random sampling) comprised 30 healthy children and 49 healthy adults, both recruited from the general population. The group of cases included a total of 76 hemophilia patients and the group of controls a total of 79 participants. The mean age of participants was 26.1 years (SD 14.4) with the youngest participant being 4 years and the oldest 58 years.

For comprehensive comparison, the following aspects of dental health/disease were considered: overall caries experience, dental treatment experience, unmet dental treatment needs and the presence of functional dentition. All clinical dental assessments were based on 28 permanent teeth (third molars not considered) and on 20 deciduous teeth (full deciduous dentition). One examiner (R.Ž.) assessed dental health or disease in both dentitions employing the WHO Criteria for Oral Health Surveys [28]. The overall caries experience was measured by employing two commonly used indices: the ''DMFT'' measuring the total number of decayed, filled and missing teeth in the permanent dentition and the

Table 1 – Dental health or disease related outcomes and their calculations.

Dental health/disease outcomes	Calculations
Ratio.dmft – an overall caries experience in the deciduous dentition	(number of decayed, missing and filled deciduous teeth/number of deciduous teeth) × 100
Ratio.DMFT – an overall caries experience in the permanent dentition	(number of decayed, missing and filled permanent teeth/number of permanent teeth) × 100
Ratio.ft – treatment experience in the deciduous dentition	(number of filled deciduous teeth/number of deciduous teeth) × 100
Ratio.FMT – treatment experience in the permanent dentition	(number of missing and filled permanent teeth/28) × 100
Ratio.dt – unmet treatment need in the deciduous dentition	(number of deciduous teeth with decay/number of deciduous teeth present) × 100
Ratio.DT– unmet treatment need in the permanent dentition	(number of decayed permanent teeth/number of permanent teeth present) × 100
T-Health Index for subjects ≥12 years (permanent dentition)	Assigning "1.0" for a sound tooth, "0.2" for a filled tooth, "0.1" for a decayed tooth and "0" for a missing tooth. A total for a permanent dentition is calculated by summing the weights of individual teeth [33]

"dft" assessing the total number of decayed and filled teeth in the deciduous dentition. Missing primary incisor teeth for children aged 5 years and older were considered exfoliated, thus these were not included in the assessment of overall caries experience in the deciduous dentition (dft). Given there were varying numbers of either deciduous or permanent teeth present in mouths of participants, we standardized all dental health or disease related outcomes by calculating standardized ratios. For calculations of these ratios refer to Table 1.

Individual plaque levels were used as a proxy measure to assess the quality of oral hygiene and for each participant the Quantitative Plaque Percent Index (P% index) was calculated. This index expresses the area on a tooth that is covered with plaque as a percentage of the total tooth area. Dental plaque was stained with a disclosing tablet, and then after rinsing the mouth with water, photos of the stained plaque attached to the labial and buccal surfaces of the premolars and molars were taken. The photographs of individual teeth were analyzed using the Adobe Photoshop software program. The number of pixels was calculated for both the area of the tooth covered with the disclosed plaque and for the total tooth area. The Individual Quantitative Plaque Percent Index was calculated by summing the % plaque indices of each tooth and then dividing this number by the number of teeth assessed. In this way, a 0% plaque score indicates an individual without dental plaque while a plaque score of 100% indicates an individual who has labial and buccal surfaces completely covered with dental plaque.

For each subject, the stimulated salivary flow rate, buffer capacity and salivary levels of caries-causing bacteria were assessed. Saliva was collected in a plastic vial. Each vial was weighed prior to saliva collection and again afterwards the vial containing the saliva was weighed. The difference in weight of the vial with and without saliva divided by the time needed to collect the saliva was recorded as the salivary flow rate in milliliters per minute. Salivary buffer capacity was determined with the CRT Buffer Test (Ivoclar Vivadent) and salivary bacterial counts were assessed using the CRT Bacteria Kit (Ivoclar Vivadent), both according to the manufacturer's recommendations. To facilitate blind assessments, both the salivary buffer capacity strips and bacteriological images were photographed. The saliva's buffer capacity was estimated colorimetrically as low, medium or high based on the manufacturer's recommended standards. For the estimation of *Streptococcus mutans* and *Lactobacilli* levels in stimulated saliva, agar plates for growing *Streptococcus mutans* and for growing *Lactobacilli* were thoroughly wetted with stimulated saliva and subsequently incubated at 37 °C for 48 h. After removing the vials from the incubator, the colonies of bacteria were photographed.

A structured questionnaire included questions about the education and occupation of adult participants and for the child participants, similar information was collected from their parents. The questionnaire also included a number of diets, oral self-care and dental-visit related questions. Measurements of the study variables are presented in the first column of Table 2.

The SPSS statistical software program version 21.0 was used for all statistical analyses. The bivariate analyses were used: (1) to test the quality of matching between the cases and controls (chi-square test/Fisher exact test), (2) to examine the intraexaminer reliability of clinical assessments (intraclass correlation) and (3) to compare the distributions of different dental health or disease-related determinants between patients with hemophilia and their matched controls (independent sample *t* test, chi-square or Fisher exact test). Linear multiple regression analyses examined the joint effect of caries-related determinants in relationship to different standardized dental health or disease related outcomes. The threshold for all statistical tests was set at $P < 0.05$.

3. Results

The matching for age was assessed with the Fisher exact test and the matching for residence was assessed with the chi-square test. Both statistical tests showed were not significant differences, indicating that the matching of cases with controls was successful. The intraexaminer reliability was assessed by comparing duplicate clinical examinations of 20 subjects which had been performed two or more days apart and also by assessing 20 randomly selected digital images twice. All intraclass correlation coefficients were

Table 2 – Risk determinants – comparisons between hemophiliacs and healthy children.

Determinants	Healthy controls		Hemophilia patients		P values (95% CI)
	n	Mean ± SD	n	Mean ± SD	
Comparison of means					
Dental plaque levels %	30	28.2 ± 15.2	27	32.0 ± 20.2	0.430 (−13.2; 5.7)
Salivary flow rate[a]	30	1.0 ± 0.5	25	0.9 ± 0.5	0.520 (−0.2; 0.3)
Comparison of proportions	n	%	n	%	P values
Salivary buffer capacity[a]					
Low	1	3.3	3	11.1	0.509
Moderate	14	46.7	11	40.7	
High	15	50.0	13	48.1	
Salivary bacteriology[a]					
S. mutans and *Lactobacilli* low	1	3.3	7	25.9	0.019
S. mutans and *Lactobacilli* medium	16	53.3	15	55.6	
S. mutans and *Lactobacilli* high	13	43.3	5	18.5	
Family's occupation					
Low	2	6.7	8	29.6	0.022
Medium	11	36.7	12	44.4	
High	17	56.7	7	25.9	
Parental education					
High school or lower	2	6.7	13	48.2	0.010
College or incomplete university	9	30.0	7	25.9	
University or higher	19	63.3	7	25.9	
Socioeconomic status (combined measure)					
Low	1	3.3	9	33.3	0.004
Medium	13	43.3	12	44.4	
High	16	53.3	6	22.2	
Tooth brushing frequency					
Non daily	4	13.3	6	22.2	0.297
Everyday	26	86.7	21	77.8	
Use of fluoridated toothpaste					
No	2	6.7	5	18.5	0.208
Do not know	16	53.3	9	33.3	
Yes	12	40.0	13	48.1	
Gum bleeding at rest					
No	30	100.0	26	96.3	0.474
Yes	0	0.0	1	3.7	
Gum bleeding during tooth brushing					
No	23	76.7	17	63.0	0.201
Yes	7	23.3	10	37.0	
Continues brushing despite bleeding					
No	19	63.3	13	48.1	0.188
Yes	11	36.7	14	51.9	
Flossing of teeth					
No	20	66.7	26	96.3	0.005
Yes	10	33.3	1	3.7	
Number of meals daily					
<3 meals	4	13.3	2	7.4	0.346
3 meals	18	60.0	13	48.1	
>3 meals	8	26.7	12	44.4	
Snacking between meals daily					
No	2	6.7	1	3.7	0.882
<3 times	15	50.0	14	51.9	
>3 times	13	43.3	12	44.4	
Consumption of soft drinks daily					
No	4	13.3	5	18.5	0.809
<3 times	19	63.3	15	55.6	
>3 times	7	23.3	7	25.9	
Last dental visit					

Table 2 (*Continued*)

Determinants	Healthy controls		Hemophilia patients		*P* values (95% CI)
	n	Mean ± SD	*n*	Mean ± SD	
Never or >1 year ago	4	13.3	8	29.6	0.119
Within the last year	26	86.7	19	70.4	
Reason for the last dental visit					
Pain or dental problem	2	6.7	6	22.2	0.384
Invitation from a dentist	1	3.3	1	3.7	
Follow-up treatment	11	36.7	7	25.9	
Preventive reason	16	53.3	13	48.1	
Dental pain					
No	22	73.3	14	51.9	0.080
Yes	8	26.7	13	48.1	

Independent sample *t* test/Mann Whitney *U* test for comparing means ± SD and chi-square test/Fischer exact test for comparing proportions.
[a] Salivary assessments could not be completed in a few patients.

above 0.900 ($P < 0.001$), indicating that intraexaminer reliability was satisfactory.

Table 2 compares the distribution of different dental health or disease-related determinants among the children and Table 3 presents similar comparisons among the adults. Although the mean and SD of dental plaque levels were higher in children with hemophilia, this difference was not statistically significant. There were no statistically significant differences between hemophiliacs and healthy children regarding salivary buffer capacity but salivary levels of caries-associated bacteria were higher in controls than in hemophilia patients. All socioeconomic status (SES) related aspects differed between the two groups with hemophiliac children being from lower SES families than their counterparts without this medical condition. Only one child with hemophilia reported gum bleeding at rest while none of the other children had this problem. Although there was no statistically significant difference between the study groups, a relatively high proportion of children, namely 23% of healthy children and 37% of hemophiliacs, noted that their gums bled while tooth brushing and high proportions of children in both groups reported that they continued brushing despite gum bleeding. There was a statistically significant difference in flossing with a higher proportion of children in the healthy group than in the cases group reporting daily flossing. None of the diet-related or dental-visit related variables differed statistically significantly between the study groups.

Similar comparisons for the adult subjects are presented in Table 3. Hemophiliacs had significantly higher dental plaque levels as compared to control subjects. There were no statistically significant differences between the adult groups in SES or in salivary parameters. Higher proportions of hemophiliacs than controls reported gum bleeding at rest or during tooth brushing and more hemophiliacs continued brushing despite bleeding as compared with controls. Diet or dental-visit patterns did not differ between the adult study groups except for the consumption of soft drinks with hemophiliacs reporting a greater consumption.

Table 4 presents the results of bivariate comparisons as they relate to different dental disease or health related indices. In the deciduous dentition, the overall caries experience (dmf) and the unmet treatment need (dt) differed statistically significantly between the hemophiliacs and their matched healthy controls (2.6 ± 2.6 vs. 6.1 ± 2.5, $P = 0.003$, and 1.4 ± 1.9 vs. 3.6 ± 2.9, $P = 0.036$, respectively). However, none of the mean standardized ratios of dental health- or disease-related outcomes differed statistically significantly between the two groups but more details can be obtained by visually comparing distributions of the study groups.

Fig. 1 illustrates the distribution in both groups regarding overall caries experience. A greater variation can be observed between the two groups concerning caries experience in deciduous dentition but no variation can be observed when comparing permanent dentitions. Fig. 2 demonstrates comparisons regarding treatment experience. Here the opposite trend can be observed, i.e. seemingly there were no variations regarding dental treatment experience in deciduous dentitions but treatment experience varied substantially in permanent dentitions. Although the majority of hemophiliacs (75%) had had less than 25% of their dentitions treated, there were a few patients (outliers presented in the right boxplot in Fig. 2) who had had most of their permanent dentitions already treated either with restorations or extractions. Fig. 3 compares the levels of unmet dental treatment needs and one can see that variation in unmet treatment needs in the deciduous dentitions are substantially larger in healthy controls than among hemophiliacs, while there was no difference in unmet treatment needs between the permanent dentitions of the two groups. Fig. 4 compares variations regarding the presence of functional dentitions and a larger degree of variation was observed in the group of hemophiliacs than in the group of controls. There were some individuals in both adult groups who had less than 10% of their functional dentition left.

Table 5 presents the results of linear multiple regression (LMR) models where the joint effect of multiple predictors was associated with different standardized dental health or disease-related ratios. In none of the LMR models explaining dental health or disease-related ratios, did the effect of a medical condition (hemophilia) present as significant when it was controlled for other known caries-associated determinants. The LMR model for the ratio of an overall caries experience in the deciduous dentitions (Ratio.dft) was statistically significant and 53.7% of variation in this model was explained jointly by multiple predictors. In this LMR

Table 3 – Risk determinants – comparisons between adult hemophiliacs and healthy controls.

Determinants	Healthy controls		Hemophilia patients		P values (95% CI)
	n	Mean ± SD	n	Mean ± SD	
Comparison of means					
Dental plaque levels %	49	21.6 ± 13.4	49	29.0 ± 15.7	0.014 (−13.2; −1.5)
Salivary flow rate[a]	49	1.2 ± 0.5	48	1.1 ± 0.5	0.269 (−0.1; 0.3)
Comparison of proportions	n	%	n	%	P values
Salivary buffer capacity[a]					
Low	7	14.3	9	18.4	0.860
Moderate	26	53.1	25	51.0	
High	16	32.7	15	30.6	
Salivary bacteriology[a]					
S. mutans and *Lactobacilli* low	6	12.5	7	14.3	0.943
S. mutans and *Lactobacilli* medium	16	13.3	17	34.7	
S. mutans and *Lactobacilli* high	26	54.2	25	51.0	
Occupation					
Low	8	16.3	15	30.6	0.248
Medium	24	49.0	20	40.8	
High	17	34.7	14	28.6	
Education					
High school or lower	18	36.8	28	57.2	0.226
College/incomplete university	11	22.4	8	16.3	
University or higher	20	40.8	13	26.5	
Socioeconomic status					
Low	8	16.3	17	34.7	0.090
Medium	21	42.9	19	38.8	
High	20	40.8	13	26.5	
Tooth brushing frequency					
Non daily	4	8.2	10	20.4	0.187
Everyday	45	91.8	39	79.6	
Use of fluoridated toothpaste					
No	5	10.2	4	8.2	0.741
Do not know	35	71.4	33	67.3	
Yes	9	18.4	12	24.5	
Gum bleeding at rest					
No	47	95.9	32	65.3	<0.001
Yes	2	4.1	17	34.7	
Gum bleeding during tooth brushing					
No	27	55.1	13	26.5	0.007
Yes	22	44.9	36	73.5	
Continues brushing despite bleeding					
No	19	38.8	10	20.4	0.038
Yes	30	61.2	39	79.6	
Flossing of teeth					
No	29	59.2	41	83.7	0.013
Yes	20	40.8	8	16.3	
Number of daily meals					
<3 meals	10	20.4	11	22.4	0.814
3 meals	21	42.9	23	46.9	
>3 meals	18	36.7	15	30.6	
Snacking between meals daily					
No	8	16.3	8	16.3	0.796
<3 times	26	53.1	23	46.9	
>3 times	15	30.6	18	36.7	
Consumption of soft drinks					
No	16	32.7	7	14.3	0.025
<3 times	22	44.9	35	71.4	
>3 times	11	22.4	7	14.3	
Last dental visit					

Table 3 (*Continued*)

Determinants	Healthy controls		Hemophilia patients		P values (95% CI)
	n	Mean ± SD	*n*	Mean ± SD	
Never or >1 year ago	14	28.6	20	40.8	0.144
Within the last year	35	71.4	29	59.2	
Reason for the last dental visit					
Pain or dental problem	19	38.8	19	38.8	1.000
Invitation from a dentist	0	0.0	0	0.0	
Follow-up treatment	15	30.6	15	30.6	
Preventive reason	15	30.6	15	30.6	
Dental pain					
No	28	57.1	24	49.0	0.544
Yes	21	42.9	25	51.0	

Independent sample *t* test/Mann Whitney *U* test for comparing means ± SD and chi-square test/Fischer exact test for comparing proportions.
[a] Salivary assessments could not be completed in a few patients.

Table 4 – Dental health and disease indicators – comparisons between hemophilia patients and healthy controls (independent sample *t* test/Mann Whitney *U* test).

Dental health/disease indices	Healthy controls		Hemophilia patients		P values (95% CI)
	n	Mean ± SD	*n*	Mean ± SD	
Overall caries experience					
dft	15	6.1 ± 2.5	11	2.6 ± 2.6	0.003 (1.3; 5.5)
Ratio.dft	15	59.4 ± 26.0	11	43.1 ± 38.8	0.208 (−9.8; 42.6)
DMFT	75	9.3 ± 7.0	72	9.4 ± 7.6	0.947 (−2.5; 2.3)
Ratio.DMFT	75	33.6 ± 24.5	72	33.7 ± 27.2	0.979 (−8.6; 8.3)
Treatment experience					
Ratio.ft	15	20.0 ± 24.8	11	23.1 ± 35.0	0.793 (−27.3; 21.1)
Ratio.FMT	75	23.7 ± 22.8	72	22.5 ± 25.3	0.766 (−6.7; 9.1)
Unmet treatment need					
Dt	15	3.6 ± 2.9	11	1.4 ± 1.9	0.036 (0.2; 4.3)
Ratio.dt	15	39.4 ± 33.0	11	19.9 ± 32.1	0.145 (−7.2; 46.7)
DT	75	2.7 ± 3.0	72	3.1 ± 4.0	0.518 (−1.5; 0.8)
Ratio.DT	75	10.6 ± 11.3	72	11.8 ± 15.2	0.575 (−5.6; 3.1)
Functional dentition (>12 years)					
T-Health Index	61	20.0 ± 5.3	61	20.4 ± 5.9	0.729 (−2.4; 1.7)

dft, number of decayed and filled deciduous teeth; Ratio.dft, standardized number of decayed and filled deciduous teeth; DMFT (number of decayed, filled and missing permanent teeth); Ratio.DMFT, standardized number of decayed, filled and missing permanent teeth; Ratio.ft, standardized number of filled deciduous teeth; Ratio.FMT, standardized number of filled and missing permanent teeth; dt, number of decayed deciduous teeth; Ratio.dt, standardized number of decayed deciduous teeth; DT, number of decayed permanent teeth; Ratio.DT, standardized number of decayed permanent teeth; T-Health Index, weighted index of functional permanent teeth.

model, the salivary levels of caries-causing bacteria ($\beta = 0.548$, $P = 0.005$), salivary flow rate ($\beta = 0.492$, $P = 0.004$), and salivary buffer capacity ($\beta = 0.414$, $P = 0.017$) were strongest predictors of overall caries experience. In contrast, the LMR model for overall caries experience in permanent dentitions was not statistically significant, and neither were any of the individual predictors. Neither treatment–experience-related models were statistically significant and nor did they comprise any significant predictors when adjusted for a number of other predictors. The LMR model of unmet dental treatment needs in the permanent dentition was highly statistically significant ($P < 0.001$) with dental plaque ($\beta = 0.330$, $P < 0.001$) and lower salivary buffer capacity ($\beta = 0.251$, $P = 0.002$) being the strongest predictors for the higher unmet dental treatment needs in permanent dentitions. The LMR model for the functional dentition was not statistically significant, nor did it have any statistically significant predictors for explaining the variations seen in the functional dentitions.

4. Discussion

The present case–control study examined caries-associated risks and related them to a number of reported caries-risk determinants and tested if patients with hemophilia have additional risk because of their medical condition compared to gender, age, and residence-matched controls from the general population. To make these assessments, a number of dental health and disease standardized ratios were calculated.

An overall finding was that for Lithuanian patients with hemophilia no risk was observed in addition to the risks for dental decay known for the population in general. Of all multivariate models for different dental disease or health

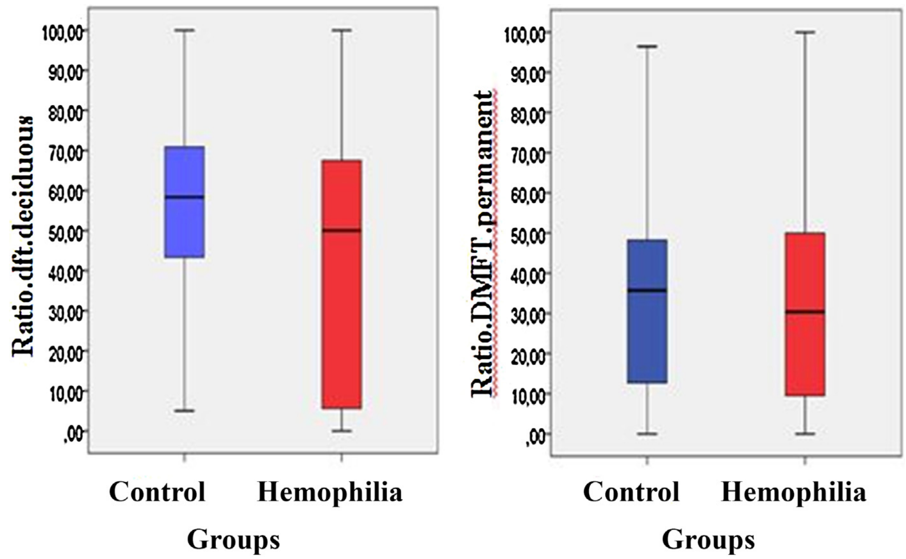

Fig. 1 – Overall caries experience in hemophiliacs and healthy controls.

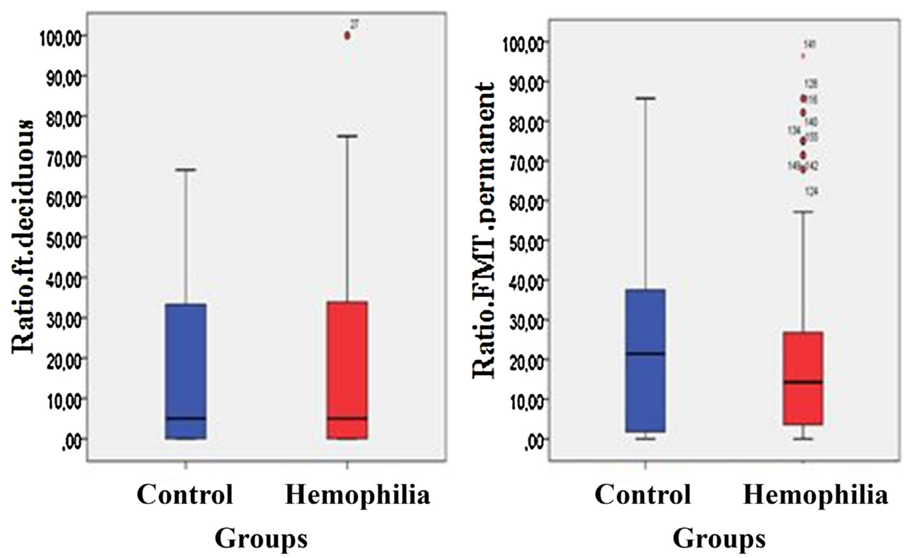

Fig. 2 – Treatment experience in hemophiliacs and healthy controls.

related outcomes, the overall caries experience for the deciduous dentition had the highest explained variance score and was highly statistically significant, where half of the variation in overall caries experience was explained by multiple predictors with the strongest being the salivary levels of caries-causing bacteria, salivary flow rate and salivary buffer capacity. These findings support the importance of host defense factors at least as they relate to maintaining healthy deciduous dentitions.

Based on the present findings, some trends could also be observed, e.g. the majority of children with hemophilia had overall better dental health in their deciduous dentitions as compared to their counterparts without hemophilia despite the hemophiliacs being from families with lower SES, which is a well-known determinant for a higher caries experience particularly in young children. It is important to consider that the only one statistically significant difference between the cases and controls was higher counts of both *Streptococcus mutans* and *Lactobacilli* in healthy controls. Seemingly, this may at least partly explain the better dental health observed in children hemophiliacs than in their healthy counterparts. This explanation can also, at least partly be supported by a finding from the present study that a higher proportion of children with hemophilia (52%) than of those without it (30%) noted that they continue brushing despite gum bleeding. Seemingly, this important knowledge about brushing was learned well by children with hemophilia or by their parents as compared to children without the disease. Despite this encouraging trend of young hemophiliac boys having better dental health than children from the general Lithuanian population, the variations seen among hemophiliacs are still worrisome as some of them had a relatively high overall caries experience.

Table 5 – Predictors of dental health/disease indices – linear multiple regression (LMR) models.

Indices	Predictors	Standardized coefficients	Significance	Tolerance
Overall caries experience				
Ratio.dft	Control vs. hemophiliacs	0.130	0.505	0.574
	Dental plaque	0.026	0.866	0.904
	Caries microorganisms	0.548	0.005	0.713
	Salivary flow rate	0.492	0.004	0.947
	Salivary buffer capacity	0.414	0.017	0.844
	Last dental visit	0.281	0.132	0.612
	SES status	0.257	0.145	0.732
	Model summary: adjusted R square = 0.537; $P = 0.003$			
Ratio.DMFT≥12 years	Control vs. hemophiliacs	0.006	0.946	0.882
	Dental plaque	0.109	0.253	0.861
	Caries microorganisms	0.096	0.293	0.948
	Salivary flow rate	0.016	0.865	0.940
	Salivary buffer capacity	0.209	0.024	0.938
	Last dental visit	0.087	0.331	0.969
	SES status	0.034	0.712	0.896
	Model summary: adjusted R square = 0.029; $P = 0.165$			
Treatment experience				
Ratio.ft	Control vs. hemophiliacs	0.277	0.337	0.566
	Dental plaque	0.024	0.920	0.815
	Caries microorganisms	0.289	0.283	0.655
	Salivary flow rate	0.314	0.209	0.769
	Salivary buffer capacity	0.106	0.661	0.787
	Last dental visit	0.160	0.561	0.612
	SES status	0.149	0.564	0.693
	Model summary: adjusted R square = 0.069; $P = 0.614$.			
Ratio.FMT (≥12 years)	Control vs. hemophiliacs	0.043	0.654	0.882
	Dental plaque	0.060	0.536	0.861
	Caries microorganisms	0.081	0.381	0.948
	Salivary flow rate	0.058	0.534	0.940
	Salivary buffer capacity	0.079	0.394	0.938
	Last dental visit	0.156	0.092	0.969
	SES status	0.074	0.441	0.896
	Model summary: adjusted R square = 0.013; $P = 0.608$			
Unmet treatment need				
Ratio.dt	Control vs. hemophiliacs	0.085	0.767	0.566
	Dental plaque	0.027	0.912	0.815
	Caries microorganisms	0.190	0.481	0.655
	Salivary flow rate	0.087	0.726	0.769
	Salivary buffer capacity	0.356	0.157	0.787
	Last dental visit	0.125	0.653	0.612
	SES status	0.055	0.832	0.693
	Model summary: adjusted R square = 0.091; $P = 0.661$			
Ratio.DT ≥12 years	Control vs. hemophiliacs	0.098	0.226	0.882
	Dental plaque	0.330	<0.001	0.861
	Caries microorganisms	0.032	0.679	0.948
	Salivary flow rate	0.072	0.358	0.940
	Salivary buffer capacity	0.251	0.002	0.938
	Last dental visit	0.120	0.123	0.969
	SES status	0.218	0.008	0.896
	Model summary: adjusted R square = 0.279; $P < 0.001$			
Functional teeth ≥ 12 years				
T-Health Index	Control vs. hemophiliacs	0.016	0.149	0.846
	Dental plaque	0.143	0.149	0.846
	Caries microorganisms	0.031	0.737	0.954
	Salivary flow rate	0.008	0.931	0.929
	Salivary buffer capacity	0.145	0.126	0.929
	Last dental visit	0.150	0.110	0.953
	SES status	0.041	0.667	0.905
	Model summary: adjusted R square = 0.017; $P = 0.259$			

Ratio.dft, standardized number of decayed and filled deciduous teeth; Ratio.DMFT, standardized number of decayed, filled and missing permanent teeth; Ratio.dt, standardized number of decayed deciduous teeth; Ratio.DT, standardized number of decayed permanent teeth; Ratio.ft, standardized number of filled deciduous teeth; Ratio.FMT, standardized number of filled and missing permanent teeth; T-Health Index, weighted index of functional permanent teeth.

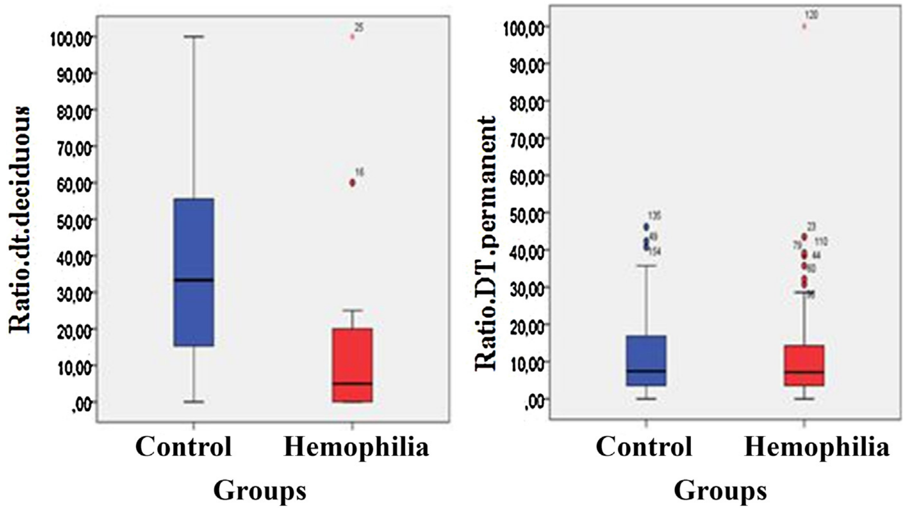

Fig. 3 – Unmet dental treatment needs in hemophiliacs and healthy controls.

However, differences in either dental health or disease outcomes disappeared when adult groups were compared. Dental caries is a cumulative life course related disease, where multiple risk determinants play a role. We observed the difference in dental caries causing bacteria and some non-significant tooth brushing differences in child samples, but not in adult samples. Consequently, future longitudinal studies in bigger samples may be needed to explain differences between children and adult samples.

Another clinically relevant finding is that a relatively high proportion of hemophiliacs reported dental pain (48%) being the reason for their last dental visit. Obviously, there is a need to increase the awareness about the importance of preventive and regular dental visits particularly among those for whom dental treatments have inherent health risks. Most importantly, the most common dental diseases (caries and periodontal disease) are preventable among hemophiliacs as well as among the general population [17].

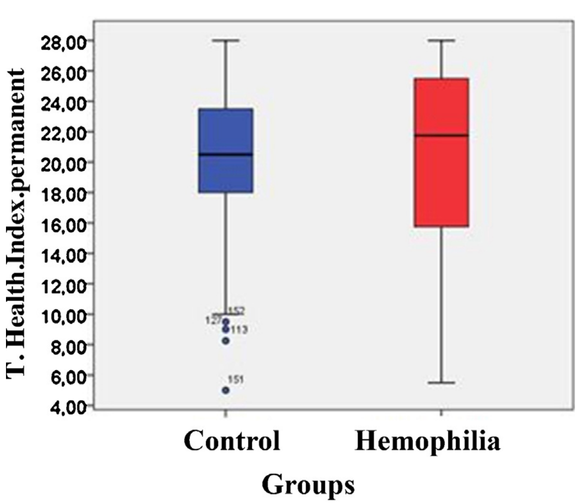

Fig. 4 – Functional dentition in hemophiliacs and healthy controls.

Concomitantly, it is important to diminish the existing barriers to accessing primary dental care that exist due to hemophiliacs being refused dental treatments because dentists do not feel confident to provide the necessary treatments for patients with bleeding disorders [29]. It is also important to emphasize that provision of operative dental treatments (fillings, crowns or bridges) or surgical treatments such as tooth extractions are secondary or tertiary prevention procedures, i.e. these dental treatments aim to restore either damaged teeth or dentitions. Implementing primary prevention aiming to reduce the need for invasive dental treatments will positively impact not only patients' lives by helping them to retain healthy dentitions but prevention of dental diseases will also have a cumulative cost-saving potential for the population as a whole as there would be no need for the hemostatic treatments which are necessary for supporting some dental treatments [29]. Thus, dental management of hemophiliacs should begin with prevention of dental disease and it is important to deliver preventive dental care as early as possible [30]. Toward an overall improvement of dental health in this vulnerable segment of population, the integration of dental care into the everyday life of hemophilia treatment centers can be recommended, which should aim toward intensive prevention of dental decay. This in turn will reduce the prevalence of dental diseases and contribute to the effective use of economic resources provided that a proactive role is taken by health authorities [31]. Hematology should also be included in the curricula of all the medical professions including medical and dental [32].

5. Conclusions

Our results showed that better dental health was observed in children with hemophilia as compared to their healthy counterparts, but were no differences in dental health between adult hemophiliacs and healthy controls randomly chosen from the general population. This study demonstrates that none of the linear multiple regression models confirmed hemophilia to be an additional caries risk when it was controlled for other caries determinants.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

[1] Brewer AK, Roebuck EM, Donachie M, Hazard A, Gordon K, Fung D, et al. The dental management of adult patients with haemophilia and other congenital bleeding disorders. Haemophilia 2003;9:673–7.
[2] Blanchete V. Inherited bleeding disorders. Bailliere's Clin Haematol 1991;4:291–332.
[3] Girolami A, Luzzatto G, Varvarikis C, Pellati D, Sartori R, Girolami B. Main clinical manifestations of a bleeding diathesis: an often disregarded aspect of medical and surgical history taking. Haemophilia 2005;11:193–202.
[4] Alpkilic BE. Dental and periodontal health in children with haemophilia. J Coagul Disord 2009;15:193–8.
[5] Sonis AL, Musselman RJ. Oral bleeding in classic hemophilia. Oral Surg Oral Med Oral Pathol 1982;53:363–6.
[6] Mielnik-Blaszczak M. Evaluation of dentition status and oral hygiene in Polish children and adolescents with congenital haemorrhagic diatheses. Int J Paediatr Dent 1999;9:99–103.
[7] Azhar S, Yazdanie N, Muhammad N. Periodontal status and IOTN interventions among young hemophiliacs. Haemophilia 2006;12:401–4.
[8] Kamppi A, Tanner T, Pakkila J, Patinen P, Jarvelin MR, Tjaderhane L, et al. Geographical distribution of dental caries prevalence and associated factors in young adults in Finland. Caries Res 2013;47:346–54.
[9] Costa SM, Martins CC, Bonfim ML, Zina LG, Paiva SM, Pordeus IA, et al. A systematic review of socioeconomic indicators and dental caries in adults. Int J Environ Res Public Health 2012;9:3540–74.
[10] Jerkovic K, Binnekade JM, van der Kruk JJ, van der Most JA, Talsma AC, van der Schans CP. Differences in oral health behaviour between children from high and children from low SES schools in The Netherlands. Community Dent Health 2009;26:110–5.
[11] Celeste RK, Nadanovsky P. Why is there heterogeneity in the effect of dental checkups? Assessing cohort effect. Community Dent Oral Epidemiol 2010;38:191–6.
[12] Thomson WM, Williams SM, Broadbent JM, Poulton R, Locker D. Long-term dental visiting patterns and adult oral health. J Dent Res 2010;89:307–11.
[13] Muirhead VE, Quinonez C, Figueiredo R, Locker D. Predictors of dental care utilization among working poor Canadians. Community Dent Oral Epidemiol 2009;37:199–208.
[14] Creske M, Modeste N, Hopp J, Rajaram S, Cort D. How do diet and body mass index impact dental caries in Hispanic elementary school children? J Dent Hyg 2013;87:38–46.
[15] Gao X, Lo EC, Kot SC, Chan KC. Motivational interviewing in improving oral health: a systematic review of randomized controlled trials. J Periodontol 2014;85:426–37.
[16] Yokoyama Y, Kakudate N, Sumida F, Matsumoto Y, Gilbert GH, Go VV. Dentists' dietary perception and practice patterns in a dental practice-based research network. PLOS ONE 2013;8:e59615.
[17] Harrington B. Primary dental care of patients with haemophilia. Haemophilia 2000;6:7–12.
[18] Rossete MR, Rezende JS, Gomes VE, Ferreira E, Ferreira E, Oliveira AC. Sociodemographic, biological and behavioural risk factors associated with incidence of dental caries in schoolchildren's first permanent molars: a 3-year follow-up study. Eur J Paediatr Dent 2013;14:8–12.
[19] Ziebolz D, Stuhmer C, Hornecker E, Zapf A, Mausberg RF, Chenot JF. Oral health in adult patients with congenital coagulation disorders – a case control study. Haemophilia 2011;17:527–31.
[20] Sonbol H, Pelargidou M, Lucas VS, Gelbier MJ, Mason C, Roberts GJ. Dental health indices and caries-related microflora in children with severe haemophilia. Haemophilia 2001;7:468–74.
[21] Ito A, Hayashi M, Hamasaki T, Ebisu S. Risk assessment of dental caries by using classification and regression trees. J Dent 2011;39:457–63.
[22] Laguna P, Klukowska A. Management of oral bleedings with recombinant factor VIIa in children with haemophilia A and inhibitor. Haemophilia 2005;11:2–4.
[23] Patton LL. Bleeding and clotting. In: Greenberg MS, Glick M, editors. Burket's oral medicine. Diagnosis and treatment. 10th ed. Hamilton: BC Decker; 2003. p. 454–78.
[24] Hicks J, Garcia-Godoy F, Flaitz C. Biological factors in dental caries: role of saliva and dental plaque in the dynamic process of demineralization and remineralization (part 1). J Clin Pediatr Dent 2003;28:47–52.
[25] Cunha-Cruz J, Scott J, Rothen M, Mancl L, Lawhorn T, Brossel K, et al. Salivary characteristics and dental caries: evidence from general dental practices. J Am Dent Assoc 2013;144:e31–40.
[26] Sonbul H, Al-Otaibi M, Birkhed D. Risk profile of adults with several dental restorations using the Cariogram model. Acta Odontol Scand 2008;66:351–7.
[27] Ruiz MA, Montiel Company JM, Almerich Silla JM. Evaluation of caries risk in a young adult population. Med Oral Patol Oral Cir Bucal 2007;12:E412–8.
[28] WHO.. Oral Health Surveys. Basic Methods. 3rd ed. 1987.
[29] Kalsi H, Nanayakkara L, Pasi KJ, Bowles L, Hart DP. Access to primary dental care for patients with inherited bleeding disorders. Haemophilia 2012;18:510–5.
[30] Boyd D, Kinirons M. Dental caries experience of children with haemophilia in Northern Ireland. Int J Paediatr Dent 1997;7:149–53.
[31] Brewer AK. Advances in minor oral surgery in patients with congenital bleeding disorders. Haemophilia 2008;14:119–21.
[32] Chuansumrit A. Treatment of haemophilia in the developing countries. Haemophilia 2003;9:387–90.
[33] Bernabe E, Suominen-Taipale AL, Vehkalahti MM, Nordblad A, Sheiham A. The T-Health index: a composite indicator of dental health. Eur J Oral Sci 2009;117:385–9.