VILNIUS UNIVERSITY

RŪTA ŽALIŪNIENĖ

DIFFERENT ASPECTS OF ORAL HEALTH, DENTAL TREATMENT NEEDS AND ORAL HEALTH-RELATED QUALITY OF LIFE IN LITHUANIAN PATIENTS WITH HAEMOPHILIA – A CASE CONTROL STUDY

Summary of Doctoral Dissertation

Biomedical sciences, Odontology (07B)

Vilnius, 2016

The thesis was prepared at Vilnius University during 2011 – 2016.

The dissertation is defended extramurally.

Scientific consultant:

Prof. Dr. Vytaute Peciuliene (Vilnius University, Biomedical Sciences, Odontology – 07B)

The dissertation will be defended at the Research Board for Odontology of Vilnius University:

Chairman:

Prof. Dr. Algirdas Utkus (Vilnius University, Biomedical Sciences, Medicine – 06B)

Members:

Prof. Dr. Una Soboleva (Riga Stradins University, Biomedical Sciences, Odontology – 07B)

Prof. Dr. Vytautas Kasiulevičius (Vilnius University, Biomedical Sciences, Medicine – 06B)

Assoc. Prof. Dr. Laura Linkevičienė (Vilnius University, Biomedical Sciences, Odontology – 07B)

Assoc. Prof. Dr. Vygandas Rutkūnas (Vilnius University, Biomedical Sciences, Odontology – 07B)

The dissertation will be defended at the open meeting of the Research Board of Odontology on the 24th of May, 2016, at 12 p.m. in the Main lecture hall of the Faculty of Medicine, Vilnius University.

Address: M.K.Čiurlionio str. 21, LT – 03101 Vilnius, Lithuania.

The summary of the dissertation has been sent out on the 22nd of April, 2016.

The dissertation is available in the library of Vilnius University and Vilnius University website: *http://www.vu.lt/lt/naujienos/ivykiu-kalendorius*

VILNIAUS UNIVERSITETAS

RŪTA ŽALIŪNIENĖ

HEMOFILIJA SERGANČIŲ ASMENŲ BURNOS SVEIKATOS BŪKLĖS, GYDYMO REIKMIŲ IR BURNOS SVEIKATOS NULEMTOS GYVENIMO KOKYBĖS VERTINIMAS LIETUVOJE

Daktaro disertacijos santrauka

Biomedicinos mokslai, odontologija (07B)

Vilnius, 2016

Disertacija rengta 2011-2016 metais Vilniaus universitete.

Disertacija ginama eksternu.

Mokslinė konsultantė – prof. dr. Vytautė Pečiulienė (Vilniaus universitetas, biomedicinos mokslai, odontologija – 07B)

Disertacija ginama Vilniaus universiteto Odontologijos mokslų krypties taryboje:

Pirmininkas:

prof. dr. Algirdas Utkus (Vilniaus universitetas, biomedicinos mokslai, medicina – 06B)

Nariai:

prof. dr. Una Soboleva (Rygos Stradinio universitetas, biomedicinos mokslai, odontologija – 07B)

prof. dr. Vytautas Kasiulevičius (Vilniaus universitetas, biomedicinos mokslai, medicina – 06B)

doc. dr. Laura Linkevičienė (Vilniaus universitetas, biomedicinos mokslai, odontologija – 07B)

doc. dr. Vygandas Rutkūnas (Vilniaus universitetas, biomedicinos mokslai, odontologija – 07B)

Disertacija ginama viešame Odontologijos mokslo krypties tarybos posėdyje 2016 m. gegužės 24 d. 12 val. Vilniaus universiteto Medicinos fakulteto Didžiojoje auditorijoje.

Adresas: M.K.Čiurlionio 21, LT – 03101 Vilnius.

Disertacijos santrauka išsiųsta 2016 metų balandžio mėn. 22 d.

Su disertacija galima susipažinti Vilniaus universiteto bibliotekoje ir VU interneto svetainėje adresu: *http://www.vu.lt/lt/naujienos/ivykiu-kalendorius*

ABREVIATIONS

AD	–	Administrative District
CCD	–	Congenital Coagulation Disorders
COHQoL	–	Child Oral Health Quality of Life Questionnaire
IOTN	–	Index of Orthodontic Treatment Need
LMR	–	Linear Multiple Regression Models
OHIP-14	–	Oral Health Impact Profile
PMA	–	Clinical Index for Gingivitis
SES	–	Socio-economic Status
WHO	–	World Health Organization
Ratio.dft	–	Standardized Number of Decayed and Filled Deciduous 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
Ratio.dt	–	Standardized Number of Decayed Deciduous Teeth
Ratio.DT	–	Standardized Number of Decayed Permanent Teeth
FST	–	Number of Sound and Filled Permanent Teeth
Ratio.FST	–	Standardized Number of "FST"

1. INTRODUCTION

1.1 Research question and it‘s relevance

Oral health is an integral part of general health. In 2010 it was reported that 3.9 billion people all around the world encounter oral health problems. Despite the joint efforts of the World Health Organization (WHO) and different national authorities to improve the existing situation, expected reduction in the prevalence of oral diseases was not achieved and this problem still remains a global public health problem in both developed and developing countries (1, 2). It is important to acknowledge that dental caries, the most prevalent oral disease, which began in the early childhood, continues to accumulate throughout the life course of individuals. As data shows, 60–90% of school-aged children and almost 100% of adults are affected by dental caries and apparently it will continue to be a major oral health problem (3). Another prevalent oral health problem is periodontal disease which maybe an additional reason for the loss of the teeth (4, 5).

In order to develop and implement effective and comprehensive national oral disease prevention programs, information should be available about the current oral health status and its related determinants in specific populations including patients with diagnosed systemic diseases. One group of systemic diseases is congenital hemorrhagic disorders to which haemophillia belongs. Haemophilia is a rare life-threatening bleeding disorder related to the deficiency of several factors: VIII (Haemophilia A), IX (Haemophilia B) and XI (Haemophilia C) (6). The Haemophilia A and the Haemophilia B are inherited as X–linked reccessive traits. The Haemophilia A is found in 80–85% of haemophilia patients with an estimated frequency of 1 in 5000–10 000 of males, while the Haemophilia B is found in 10–15% of haemophilia patients with an estimated frequency 1 in 30 000–50 000 of males (7, 8). The Haemophilia C is inherited as an autosomal trait, it is not gender related and it has a frequency of 1:100 000 in a general population (9).

The severity of a disease of both the Haemophilia A and B associates with the activity of factors in the blood and is divided as follows: severe when factor levels are less than 1%, moderate - with the range from 1 to 5% and mild – 6 to 40% (10). Up to 30% of mild forms of haemophillia cases are first diagnosed following an episode of

uncontroled oral bleeding after dental treatment procedures or a traumatic injury. Therefore, it is important to increase awareness about haemophilia patients among dental professionals. Most importantly, individuals with moderate and severe forms of haemophilia generally have a higher risk of spontaneous and life-threatening musculoskeletal bleedings. Common sites of bleeding include knee, ankle and elbow joints. Result of this is a joint pain, swelling and decreased range of motion with uncontrolled repeated bleedings potentially leading to a permanent joint damage (11). Consequently, a replacement of factors VIII or IX by an intravenous infusion is a mandatory treatment in haemophilia patients.

In thinner regions of the oral mucosa, there are a number of enlarged capillaries near the surface. Therefore, even a minor trauma during toothbrushing, eating etc. could cause bleedings. This might be one of the reasons why patients with haemophilia avoid meticulous oral self-care (12). Another reported difficulty of haemophilia patients is accessing professional dental care with a well-known patient-related barrier being fear of dental treatments (12). In haemophillia patients, the disease-specific risks and patient barriers, both potentially contribute to patients' deteriorating oral health and this leads to an increasing need for more invasive and complex dental treatments (13). In order to secure complex dental treatment procedures of such patients, additional costs will be required due to the need of factor replacement prior to the complex treatments; such necessary supportive treatments may be even unavailable in some locations (14). It is also important to consider that dentists-associated barriers exist and are related to dentists' lack of knowledge and their ability to manage haemophilia patients (12). Due to the potential complications, Lithuanian dentists tend not to treat haemophilia patients and send these patients to the specialized clinics. As a consequence, access to the primary dental care for such patients becomes limited. Therefore, we may expect that Lithunian haemophilia patients may have higher levels of oral diseases as compared to their counterparts without haemophilia.

Congenital hemorrhagic disorders comprise only a small proportion of systemic inheritary diseases. Therefore, this could be an explanation why only a few studies analysing oral health problems among haemophilia patients have been done so far. A higher caries experience is commonly associated with lifestyle and reduced host resistance. Thus, it is important to examine whether haemophilia could be an additional

risk for dental caries. Azhar et al. reported a higher caries experience among persons with severe forms of Haemophilia A or B (15). Understanding oral health and dental treatment needs in haemophilia patients could help us to establish protocols and guidelines for the primary oral health prevention, as well for the secondary prevention (dental treatments), both might be helpful to reduce overall dental treatment needs and their related risks (14). A number of caries-related determinants have been established. The frequent consumption of carbohydrate-containing products and deficient oral hygiene are main well-established etiological factors associated with dental caries (16, 17). Low social economic status has been associated with higher caries risk and has been linked to more frequent consumption of sugar-containing foods or drinks, lack of oral hygiene and infrequent dental visits (18, 19).

1.2 The goal and objectives

The goal of the present study was to examine different aspects of oral health, its determinants, dental treatment needs and oral health-related quality of life in Lithuanian haemophilia patients.

The specific objectives were as follows:

1. To estimate caries experience, dental treatment experience, unmet dental treatment needs and presence of functional dentitions in haemophilia patients and compare their oral health-related outcomes to similar outcomes of matched controls.
2. To examine the periodontal status of haemophilia patients and compare these patients to their matched controls.
3. To evaluate the orthodontic treatment needs in haemophilia patients and compare them to their matched controls.
4. To examine a number of oral health-related determinants in haemophilia patients.
5. To compare oral health-related quality of life in patients with and without haemophilia.

1.3. Scientific novelty and relevance

There were no previous Lithuanian studies evaluating different aspects of oral health and its related determinants among haemophilia patients. In addition, there have been only a few studies from other countries which studied oral health of this vulnerable segment of population. The review of previous evidence shows some contradictory results. Therefore, the present study might provide new evidence which may have both: scientific value and clinical implications.

Prior to the planning of prophylactic programs, different aspects of oral health, dental treatment needs and oral health related quality of life must be evaluated in haemophilia patients (both children and adults). Each haemophilia patient participating in the present study was provided with an individualized preventive and dental treatment plan. In addition, a new interdisciplinary team-based collaboration has been established between general dental practitioners, dental specialists, general medical practitioners and hematologists. The results of the present study will also be useful for the further planning and organizing oral health prevention programs in Lithuania including specific guidelines for the dental management of haemophilia patients.

2. MATERIAL AND METHODS

The study was approved by the National Lithuanian Ethics Board (#158200-11-425-119). The present case control study included a group of cases (haemophilia patients) and a group of matched controls with a total of 155 study participants. Census sampling (all cohort of haemophilia patients included) was used for recruiting haemophilia cases. The register of haemophilia patients comprised all haemophilia patients four years or older (N=76). The similar size control group (N=79) was chosen from the general Lithuanian population by randomly selecting subjects from five administrative regions of Lithuania and matching with cases was based on gender, age and place of residence.

The data for both study groups was collected from November, 2011 to March, 2013. For the clinical evaluation, a total of 28 teeth (third molars were not included) in a

permanent dentition and a total of 20 teeth of the deciduous dentition were examined. Due to natural exfoliation, missing primary incisor teeth for children aged five years and older were not included in the assessment of overall caries experience in the deciduous dentition. Clinical and radiographic evaluations were done in dental clinics by the same examiner. Three aspects of oral health were evaluated for each participant: dental health, periodontal health and orthodontic status. The following aspects of dental health were considered: overall caries experience, dental treatment experience, unmet dental treatment needs and the presence of functional dentitions. In order to standardize all dental health or disease related outcomes based on varying numbers of teeth, the standardized ratios were calculated (Table 1).

To assess the quality of oral hygiene for each participant the Quantitative Plaque Percent Index (P% index) was calculated (20). After staining dental plaque with a disclosing tablet and rinsing the mouth with water, photos of the premolars and molars were taken. Adobe Photoshop Elements software program was used for digitally assessing oral hygiene levels employing quantification of dental plaque scores as a proxy measure of oral hygiene. These digital calculations of existing dental plaque levels were done in a following way. The number of pixels in photos was calculated for both: the area of the disclosed plaque and for the total tooth estimated area (both areas with and without dental plaque). The total quantitative dental plaque P% index was calculated by averaging the % plaque indices of all teeth. In this way, a 0% plaque score indicated no dental plaque while a 100% plaque score indicated an individual had all labial and buccal surfaces of teeth completely covered with dental plaque.

For each subject, a stimulated salivary flow rate, salivary buffer capacity and salivary levels of caries-causing bacteria were also assessed. The salivary buffer capacity was determined employing the CRT Buffer Test (Ivoclar, Vivadent), and the salivary bacterial counts of *Streptococcus mutans* or counts of *Lactobacilli* were assessed using the CRT Bacteria Kit (Ivoclar, Vivadent), both tests were employed following the manufacturer's recommendations. The saliva's buffer capacity was estimated calorimetrically as low, medium or high by comparing subject’s tests with the manufacturer's recommended standards.

Table 1. Adjusted dental health or disease related outcomes and their calculations

Dental Health-Related Outcomes	Calculations
Ratio.dft – an overall caries experience in the deciduous dentition	(a number of decayed and filled deciduous teeth / a total number of deciduous teeth)×100
Ratio.DMFT – an overall caries experience in the permanent dentition	(a number of decayed, missing and filled permanent teeth/a total number of permanent teeth)×100
Ratio.ft – treatment experience in the deciduous dentition	(a number of filled deciduous teeth/ a total number of deciduous teeth)×100
Ratio.FMT – treatment experience in the permanent dentition	(a number of missing and filled permanent teeth/ a total number of permanent teeth present)×100
Ratio.dt – unmet treatment need in the deciduous dentition	(a number of deciduous teeth with decay/a number of deciduous teeth present)×100
Ratio.DT – unmet treatment need in the permanent dentition	(a number of decayed permanent teeth/a total number of permanent teeth present)×100
T-Health Index for subjects ≥ 12 years (permanent dentition) (21)	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

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 or caregivers. Socio-economic status (SES) of the study participants was divided into low, medium and high SES based on education and occupation (22). In addition, the questionnaire also inquired about diet, oral self-care and dental visits.

For the clinical examination of periodontal health, the clinical PMA index was used and this index comprises assessment of three components (P-papilla, M-marginal gingiva, A-attached gingiva), each scored from 0 to 5, depending on the severity of inflammation with `0` indicating no inflammation and `5` refering to the most severe inflammation (23). Due to ethical considerations, only panoramic radiographs were used for the assessment of alveolar bone loss. The evaluation of periodontal status was carried out under the standardized conditions. The alveolar bone loss was evaluated for each tooth site, where the distance between the cemento-enamel junction of the tooth and alveolar crest was measured and expressed as the proportion of bone loss relative to the

length of the root (24). For the estimation of the orthodontic treatments needs, the Index of Orthodontic Treatment Need (IOTN) was used by evaluating oral photos in adittion to the panoramic X-rays (25). The IOTN has five grades, ranging from `1` (no need for orthodontic treatments) to `5` (substantial need for orthodontic treatments).

The Oral Health Impact Profile (OHIP-14) was used to examine and compare the oral health-related quality of life among adult patients with and without haemophilia (26). The OHIP-14 uses a 5-point Likert scale and covers seven quality of life-related aspects such as functional limitations, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap. For the calculation of the total OHIP scores, the scores of all 14 items are summed and the possible range is 0-56. For our analyses, each of the OHIP-14 answers were dichotomized into either a score 0 indicating no impact on the quality of life scores or into a score 1 indicating that there an impact on the quality of life. Due to this dichotomization, the theoretical range of the total adjusted OHIP-14 scores ranged from 0 to 14.

For children, the quality of life was measured employing a different questionnaire. Subsequently, the impact of oral and orofacial conditions on the functional, emotional, and social well-being on children and their families was evaluated using the Child Oral Health Quality of Life Questionnaire (COHQoL), which consists of a Parental Caregiver Perceptions Questionnaire, a Family Impact Scale and three age-specific questionnaires for children (27, 28, 29, 30). These questionnaires were completed either by parents of children (4–8 years old) or by older children themselves. Impact on the family‘s quality of life was reported only by parents. The COHQoL questionnaire included 55 questions which were organized into seven domains: general health symptoms (N=6 questions), oral symptoms (N=6 questions), impact on food intake (N=6 questions), impact on emotional well-being (N=7 questions), impact to social life (N=9 questions), impact on school life (N=7 questions), impact to family life (N=14 questions). For all the questionnaire items, a four-point Likert scale was used, where answers: never and don’t know were coded as “0”, sometimes as “1”, often as “2”, and all the time as “3”. The total COHQoL score was calculated by summing the answers to all questionnaire items with a possible range 0–165, where a lower total COHQoL score indicated better oral health-related quality of life.

The SPSS 21.0 software was used for all statistical analyses with a threshold for statistical significance set at $P<0.05$. The intra-examiner 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 photo images twice. The intra-class correlation coefficients were from 0.744 to 0.971 ($P<0.001$), indicating that intra-examiner reliability was satisfactory.

The bivariate analysis was used to test the quality of matching between the cases and controls (Chi-square test or Fisher exact test) and to compare the distributions of different dental health or disease-related determinants between patients with haemophilia and their matched controls (independent sample t test, chi-square or Fisher exact test). The linear multiple regression analysis was chosen to assess the effect of caries-related determinants association with standardized dental health or disease related outcomes.

3. RESULTS

The mean age of participants was 26.1 years (SD±14.4) with the youngest participant being 4 years and the oldest being 58 years. The distribution of the study participants according to the group, the haemophilia type and its severity are presented in Table 2. The severe form of Haemophilia A was the most frequent diagnosis among both children and adults with haemophilia.

Table 2. Distribution of the study participants

Study subjects	Children (4-17 years)		Adults (18-60 years)		Total
	Number	%	Number	%	
Subjects without haemophilia (matched controls)	30	38.0	49	62.0	79 (100%)
Haemophilia patients (cases)	27	35.5	49	64.5	76 (100%)
Haemophilia A Mild	5	50.0	5	50.0	10 (100%)
Haemophilia A Moderate	3	37.5	5	62.5	8 (100%)
Haemophilia A Severe	15	31.9	32	68.1	47 (100%)
Haemophilia B Mild	0	0.0	0	0.0	0 (0%)
Haemophilia B Moderate	0	0.0	2	100.0	2 (100%)
Haemophilia B Severe	4	44.4	5	55.6	9 (100%)
Total	57	36.8	98	63.2	155 (100%)

The matching of the two study groups (cases with controls) was based by age, gender and place of residence (Table 3). Only male participants were included and the proportional distributions regarding age and a place of residence were not statistically significant between the study groups; both indicating the success of matching between the cases and controls.

Table 3. Matching of the cases and controls based on age and residency

Age Groups	Matched controls		Haemophilia Patients		Total
	Number	%	Number	%	
4-6 years	3	37.5	5	62.5	8 (100%)
7-10 years	10	71.4	4	28.6	14 (100%)
11-14 years	8	47.1	9	52.9	17 (100%)
15-17 years	9	50.0	9	50.0	18 (100%)
18-20 years	6	46.2	7	53.8	13 (100%)
21-30 years	14	50.0	14	50.0	28 (100%)
31-40 years	11	44.0	14	56.0	25 (100%)
41-50 years	15	60.0	10	40.0	25 (100%)
51-60 years	3	42.9	4	57.1	7 (100%)
Total	79	51.0	76	49.0	155 (100%)
Significance #1		P=0.794			
Administrative Districts (AD)					
AD 1	22	56.4	17	43.6	39 (100%)
AD 2	27	50.9	26	49.1	53 (100%)
AD 3	13	48.1	14	51.9	27 (100%)
AD 4	8	50.0	8	50.0	16 (100%)
AD 5	9	45.0	11	55.0	20 (100%)
Total	79	51.0	76	49.0	155 (100%)
Significance #2		P=0.933			

1 Chi Squared Test; #2 Fischer Exact Test

Different dental health-related outcomes are compared between haemophilia patients and their matched controls in Table 4. Analyses showed that haemophilia children had more than twice lower overall caries experience as compared to their matched controls, but there were no statistically significant differences between the cases and controls in their overall caries experience in permanent dentitions (Table 4). Regarding the treatment experience only one non-significant associations were observed: the mean number of deciduous filled teeth was lower in haemophilia children than in children without haemophilia. The unmet dental treatment needs in the deciduous

dentition were significantly lower in children with haemophilia as compared to their counterparts from the control group.

Table 4. Dental health and disease – comparisons between haemophilia patients and their matched controls

Dental Health Indices #	Matched Controls		Haemophilia 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					
ft	15	2.5±2.9	11	1.3±1.9	0.237 (-0.8; 3.2)
Ratio.ft	15	20.0±24.8	11	23.1±35.0	0.793 (-27.3;21.1)
FMT	75	6.6±6.4	72	6.3±7.1	0.296 (-1.9; 2.5)
Ratio.FMT	75	23.7±22.8	72	22.5±25.3	0.766 (-6.7; 9.1)
Unmet Dental 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 (only for ≥12 years)					
FST	61	22.5±5.1	61	22.5±5.6	0.945 (-2.0;1.9)
Ratio.FST	61	83.8±16.1	61	83.3±18.3	0.868 (-5.7;6.7)
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 "dft"; "DMFT" (number of decayed , filled and missing permanent teeth); "Ratio.DMFT"–standardized number of "DMFT"; "dt" (number of decayed deciduous teeth); "Ratio.dt" –standardized number of "dt"; "DT" (number of decayed permanent teeth); "Ratio.DT"–standardized number of "DT"; "FST" (number of sound and filled permanent teeth); "Ratio.FST" (standardized number of "FST"); T-Health Index (weighted index of functional permanent teeth).

The mean and SD of dental plaque levels were not statistically significantly different between children with and without haemophilia (Table 5). Neither statistically significant differences were detected between children with haemophilia and children without haemophilia in salivary buffer capacity, but salivary levels of caries-associated bacteria were higher in controls than in haemophilia patients (Table 5). All socio-

economic status (SES) related aspects differed between the two groups: an overall trend was that the haemophilia children were from lower SES status family groups than their counterparts.

Table 5. Caries-associated determinants – comparisons between children with haemophilia and matched controls #

Determinants	Matched Controls		Haemophilia Patients		P values (95%CI)
Comparison of means	N	mean±SD	N	mean±SD	
Dental Plaque Levels %	30	28.2±15.2	27	32.0±20.2	0.430 (-13.2;5.7)
Salivary Flow Rate*	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*					
Low	1	3.3	3	11.1	
Moderate	14	46.7	11	40.7	0.509
High	15	50.0	13	48.1	
Salivary Bacteriology*					
S.mutans & *Lactobacilli* low	1	3.3	7	25.9	
S.mutans & *Lactobacilli* medium	16	53.3	15	55.6	0.019
S.mutans & *Lactobacilli* high	13	43.3	5	18.5	
Family's Occupation					
Low	2	6.7	8	29.6	
Medium	11	36.7	12	44.4	0.022
High	17	56.7	7	25.9	
Parents' Education					
High school or lower	2	6.7	13	48.2	
College or incomplete university	9	30.0	7	25.9	0.010
University or higher	19	63.3	7	25.9	
Socio-economic status (a combined measure)					
Low	1	3.3	9	33.3	
Medium	13	43.3	12	44.4	0.004
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	
Don't know	16	53.3	9	33.3	0.208
Yes	12	40.0	13	48.1	

Table 5, continued. Caries-associated determinants – comparisons between children with haemophilia and matched controls #

Determinants	Matched Controls		Haemophilia Patients		P values
Comparison of proportions	N	%	N	%	
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 gum 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 daily meals					
< 3 meals	4	13.3	2	7.4	
3 meals	18	60.0	13	48.1	0.346
> 3 meals	8	26.7	12	44.4	
Snacking between meals daily					
No	2	6.7	1	3.7	
< 3 times	15	50.0	14	51.9	0.882
> 3 times	13	43.3	12	44.4	
Consumption of soft drinks daily					
No	4	13.3	5	18.5	
< 3 times	19	63.3	15	55.6	0.809
> 3 times	7	23.3	7	25.9	
Time of the last dental visit					
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	
Invitation from a dentist	1	3.3	1	3.7	0.384
Follow-up treatment	11	36.7	7	25.9	
Preventive reason	16	53.3	13	48.1	
Presence of 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 Squared Test/Fischer's Exact Test for comparing proportions. * Salivary assessments could not be completed in a few patients.

The adults with haemophilia had significantly higher dental plaque levels as compared to the control subjects (Table 6). Diet or dental visit patterns did not differ between the adult study groups except for the consumption of soft drinks which was higher in the haemophilia group.

Table 6. Caries determinants – comparisons between adults with haemophilia and matched controls #

Determinants	**Matched Controls**		**Haemophilia Patients**		**P values (95%CI)**
Comparison of Means	N	mean±SD	N	mean±SD	
Dental Plaque Levels %	49	21.6±13.4	49	29.0±15.7	0.014 (-13.2;-1.5)
Salivary Flow rate*	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*					
Low	7	14.3	9	18.4	
Moderate	26	53.1	25	51.0	0.860
High	16	32.7	15	30.6	
Salivary Bacteriology*					
S.mutans & *Lactobacilli* low	6	12.5	7	14.3	
S.mutans & *Lactobacilli* medium	16	13.3	17	34.7	0.943
S.mutans & *Lactobacilli* high	26	54.2	25	51.0	
Occupation					
Low	8	16.3	15	30.6	
Medium	24	49.0	20	40.8	0.248
High	17	34.7	14	28.6	
Education					
High school or lower	18	36.8	28	57.2	
College/ incomplete university	11	22.4	8	16.3	0.226
University or higher	20	40.8	13	26.5	
Socio- economic Status					
Low	8	16.3	17	34.7	
Medium	21	42.9	19	38.8	0.090
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	
Don’t know	35	71.4	33	67.3	0.741
Yes	9	18.4	12	24.5	

Table 6, continued. Caries determinants – comparisons between adults with haemophilia and matched controls #

Determinants	Matched Controls		Haemophilia Patients		P values
Comparison of Proportions	N	%	N	%	
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	
3 meals	21	42.9	23	46.9	0.814
> 3 meals	18	36.7	15	30.6	
Snacking between meals daily					
No	8	16.3	8	16.3	
< 3 times	26	53.1	23	46.9	0.796
> 3 times	15	30.6	18	36.7	
Consumption of soft drinks					
No	16	32.7	7	14.3	
< 3 times	22	44.9	35	71.4	0.025
> 3 times	11	22.4	7	14.3	
Last dental visit					
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	
Invitation from a dentist	0	0.0	0	0.0	1.000
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 Squared Test/Fischer's Exact Test for comparing proportions. * Salivary assessments could not be completed in a few patients.

Due to small numbers in the subgroups of haemophilia patients, only two groups: one of the cases and another one of matched controls were formed for subsequent statistical analysis. A greater inter-individual variation was observed in caries experience in deciduous dentitions (Fig. 1). Dental treatment experience also varied substantially between individuals in permanent dentitions (Fig. 2).

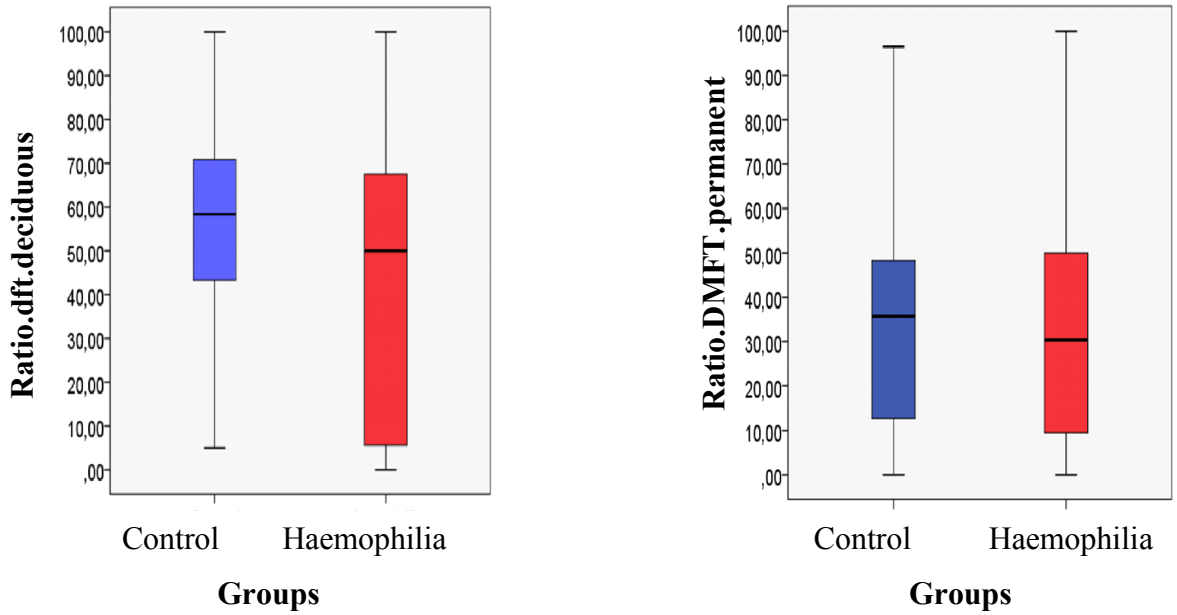

Figure 1. Overall caries experience in patients with haemophilia and matched controls

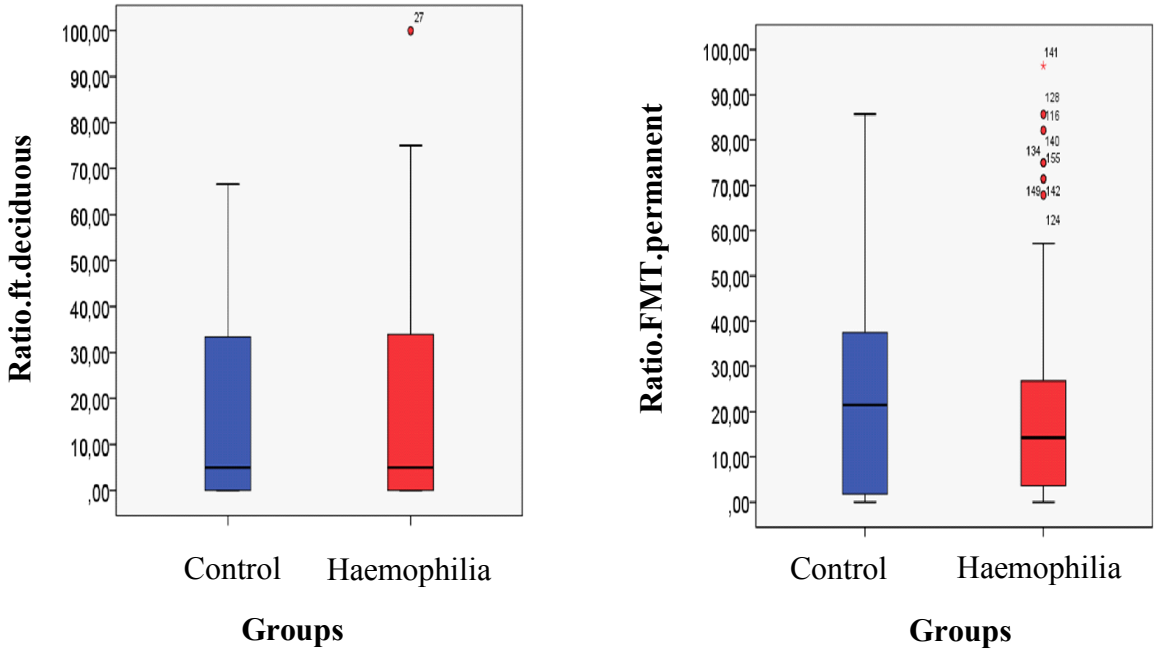

Figure 2. Treatment experience in patients with haemophilia and matched control

The inter-individual variation in the unmet dental treatment needs in the deciduous dentitions was substantially larger among controls than among the haemophilia patients, while there was no difference in the unmet dental treatment needs in the permanent dentitions between the two study groups (Fig. 3). Important finding was that there were individuals in both adult groups who had less than 10% of their functional dentition left (Fig. 4)

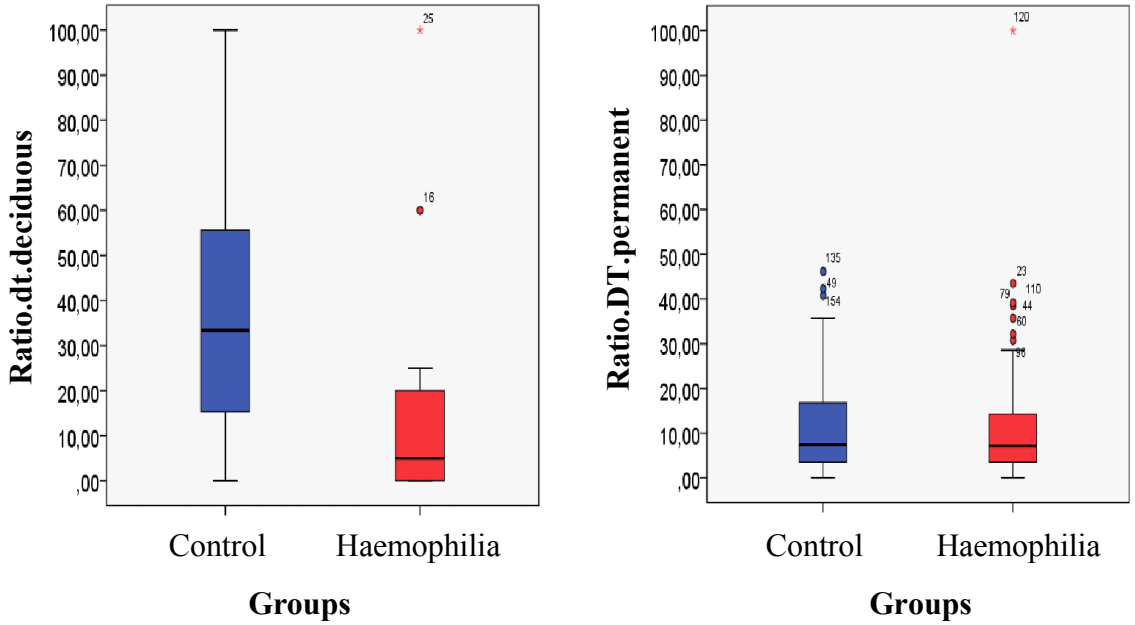

Figure 3. Unmet dental treatment needs in patients with haemophilia and matched controls

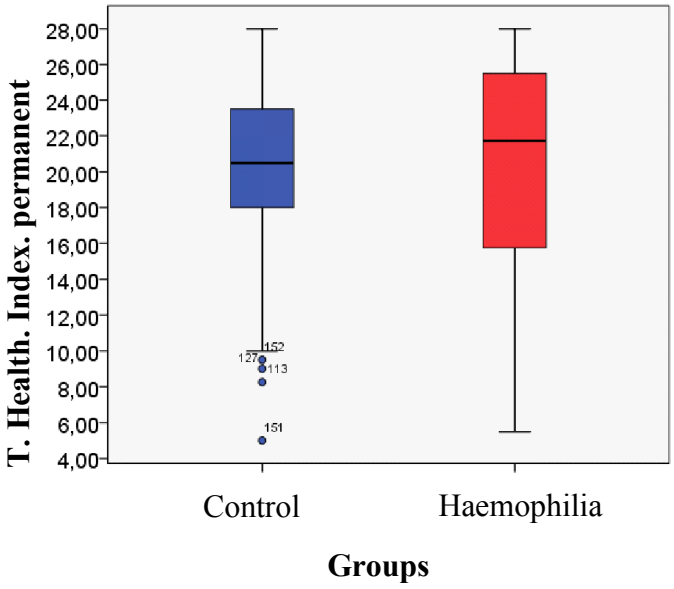

Figure 4. Functional dentition in patients with haemophilia and matched controls

Predictors of the dental health-associated outcomes were tested by linear multiple regression (LMR) models and the results of this testing are presented in Table 7.

Table 7. Determinants of dental health outcomes – linear multiple regression (LMR) models

Indices	Determinants	Standardized coefficients	Significance	Tolerance
Overall caries Experience				
Ratio.dft	Control vs Haemophiliacs	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. Haemophiliacs	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. Haemophiliacs	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. Haemophiliacs	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.			

Table 7, continued. Determinants of dental health outcomes – linear multiple regression (LMR) models

Indices	Determinants	Standardized coefficients	Significance	Tolerance
Unmet Treatment Need				
Ratio.dt	Control vs. Haemophiliacs	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	Control vs. Haemophiliacs	0.098	0.226	0.882
(≥ 12 years)	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. Haemophiliacs	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).

In none of the LMR models the medical condition (haemophilia) presented as a significant additional determinant of higher caries – associated outcomes when it was controlled for other known caries 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 sucha as: higher salivary levels of caries-causing bacteria (β=0.548, P=0.005), lower salivary flow rate (β=0.492, P=0.004) and lower salivary buffer capacity (β=0.414, P=0.017). In contrast, the LMR model for the overall caries experience in permanent dentitions was not statistically significant. The LMR model of the unmet dental treatment needs in the permanent dentitions was highly statistically significant (P<0.001) with dental plaque (β=0.330, P<0.001) and lower salivary buffer capacity (β=0.251, P=0.002) being the strongest predictors for the higher unmet dental treatment needs in permanent dentitions.

Comparisons between the study groups regarding the need for orthodontic treatments are presented in Table 8. Considering the dental health component of IOTN, 38.1% of the haemophilia patients showed the highest grades 4 or 5, 9.2% of them were defined as grade 3 and 52.7% of participants presented with the grades 1 or 2 indicating that little slight or none orthodontic treatments were needed.

Table 8. Orthodontic treatment needs – comparisons between patients with haemophilia and matched controls

Study participants	**Dental health component of IOTN**											
	Grade 1		Grade 2		Grade 3		Grade 4		Grade 5		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
Age Group: 6–13 years												
Haemophilia Patients	6	40.0	4	26.7	2	13.3	2	13.3	1	6.7	15	100
Matched Controls	12	63.1	2	10.5	3	15.8	1	5.3	1	5.3	19	100
Total	18	53.0	6	17.6	5	14.7	3	8.8	2	5.9	34	100
Significance #	P=0.234											
Age Group: 14–17 years												
Haemophilia Patients	3	30.0	4	40.0	1	10.0	2	20.0	0	0.0	10	100
Matched Controls	4	40.0	2	20.0	2	20.0	0	0.0	2	20.0	10	100
Total	7	35.0	6	30.0	3	15.0	2	10.0	2	10.0	20	100
Significance #	P=0.273											
Age Group: 18–60 years												
Haemophilia Patients	14	29.2	6	12.5	4	8.3	23	47.9	1	2.1	48	100
Matched Controls	9	18.4	10	20.4	4	8.2	25	51.0	1	2.0	49	100
Total	23	23.7	16	16.5	8	8.2	48	49.5	2	2.1	97	100
Significance #	P=0.706											

Fisher exact test

The evaluation of the needs for orthodontic treatments in the control group presented similar results to the haemophilia group. The differences between the two study groups were not statistically significant (P>0.05).

The results of periodontal comparisons are presented in Table 9. Comparisons of the PMA scores showed significant differences between the two study groups with haemophilia patients having significantly higher gingivitis scores in marginal (P=0.002) and attached (P=0.001) gingiva (Table 9). Haemophilia patients had an overall significantly worse gingival status as compared to the control subjects (P<0.05).

Table 9. Gingival status – comparisons between patients with haemophilia and matched controls

Study participants	PMA index scores					
	Papilla		Marginal		Attached	
	N	mean±SD	N	mean±SD	N	mean±SD
Haemophilia Patients	49	1.5±1.2	49	1.0±1.2	49	0.4±0.7
Matched Controls	49	1.0±0.9	49	0.5±0.6	49	0.1±0.3
Significance #	P=0.062		P=0.002		P=0.001	

Independent sample t test/Mann-Whitney U test

Based on the radiological findings, the presence of apical periodontitis was detected in 33.8% (N=24) of the haemophilia patients and in the 44.7% (N=34) of matched controls, but these prevalences did not differ significantly between the study groups (P=0.141). The level of alveolar bone loss was evaluated in the total of 2476 teeth present in a total of 98 adults. More than 42.3% of the teeth of haemophilia patients had no alveolar bone loss.

The quality of life comparisons were available for the total of 155 participants (response rate=100%). The internal consistency among different items of the Oral Health Impact Profile (OHIP-14) adult questionaire; the Cronbach's alpha was 0.876 and for the Child Oral Health Quality of Life Questionnaire (COHQoL) it was 0.804, both scores indicating a good internal consistent for the quality of life measures. Overall oral health impact on adults with and without haemofilia quality life was low. Of all, 92.9% of adult participants (N=91) reported that they never had trouble pronouncing any words, and 81.6% of them (N=80) never felt tense because of problems with their teeth, mouth or

dentures. The total OHIP-14 scores in the haemophilia group ranged from a minimum of 0 to a maximum of 31, and in the control group these scores ranged from 0 to 29. A greater variation was observed in the group of haemophilia patients than in the group of their matched controls: the overall OHIP-14 score of 75% adults with haemophilia varied from 0 to 5, and in the matched control group the range was 0–3.5 (Fig. 5). Oral health-related quality of life in the haemophilia patients group was worse, but statistical comparisons of the mean OHIP-14 scores between adult haemophiliacs (3.5±3.8) and their matched controls (2.5±3.0) were not significantly different (P=0.240).

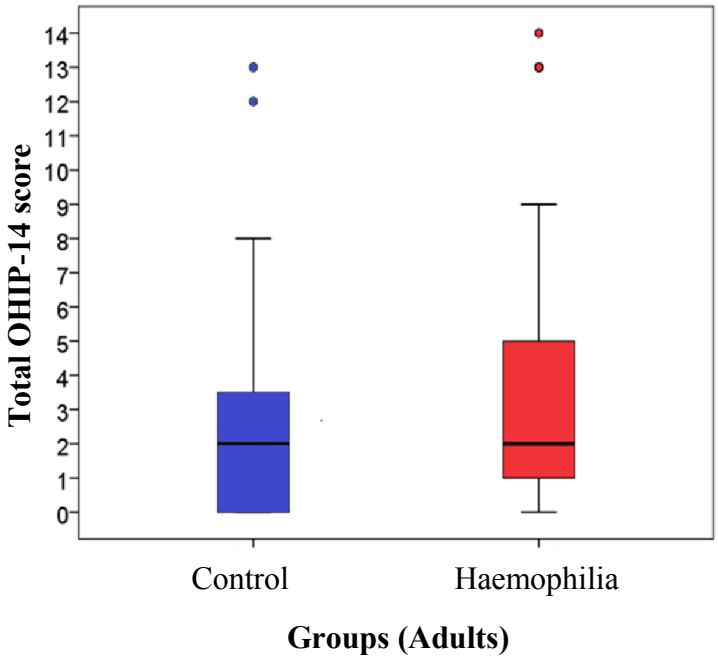

Figure 5. Oral health-related quality of life in patients with haemophilia and matched controls

The total quality of life scores (COHQoL) in the haemophilia children group ranged from 0 to 40 and in the control group from 0 to 24. In both groups, there were children who reported high impact on their general quality of life and children who also noted negative impact on laughing, eating, emotional and social well-being (Table 10). Although impact on the family‘s life due a child’s oral condition was higher in the haemophilia group (3.1±3.5) than in the control group (2.0±1.9), this difference was not significant (P=0.401). The reports of oral health-related quality of life and its seven

specific domains were not significantly different between the children with and without haemophilia (P>0.05).

Table 10. Oral health-related quality of life – comparisons between the children with haemophilia and matched controls #

COHQoL domains	Haemophilia Patients		Matched Controls		P values
	N	mean±SD	N	mean±SD	
General health symptoms	27	1.7±1.0	30	1.6±1.2	0.912
Oral symptoms	27	2.8±1.7	30	2.7±1.4	0.853
Impact to food intake	27	2.0±1.4	30	1.8±1.0	0.461
Emotional well-being	27	2.0±1.4	30	1.8±1.1	0.468
Impact to social life	27	0.7±0.7	30	0.4±0.6	0.114
Impact to school life	27	1.0±1.6	30	0.6±1.1	0.303
Impact to family life	27	3.1±3.5	30	2.0±1.9	0.401

Independent sample t test/Mann-Whitney U test

4. DISCUSSION

Dental caries is a cumulative life course-related disease, where multiple risk determinants may play an important role. The present study examined a number of caries determinants/predictors. The main research question was to find out if haemophilia poses an additional risk to caries experience.

Results of our study showed that better dental health in deciduous dentitions was observed in children with haemophilia. Of all multivariate models for different dental disease or health 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 high salivary levels of caries-causing bacteria, decreased salivary flow rate and buffer capacity. These findings support the importance of host defense factors at least as they relate to maintaining healthy deciduous dentitions. It is important to consider that the statistically significant difference between the cases and controls related to the higher counts of both *Streptococcus mutans* and *Lactobacilli* in controls. This might be at least partly explained by the fact that better dental health was observed in the haemophilia children than in their matched counterparts. This explanation can also be supported by our finding

from that a higher proportion of children with haemophilia (51.9%) than of those without it (36.7%) stated that they continue brushing despite gum bleeding. However, it is still important to take into consideration that some patients with haemophilia had a relatively high overall caries experience.

Our findings were in contrast with the findings from a similar studies performed in Egyptian children (average age 7–8 years) or in Pakistanian adolescents (average age 16 years) (15, 31). Results of these two studies contrast our findings because these two studies reported a significantly higher overall caries experience in children with haemophilia than in healthy subjects. Concomitantly, our findings are consistent with the results of studies done in Polish children and in children from Northern Ireland (32, 33). Possibly, haemophilia children in Poland or in Ireland share more commonalities with the haemophilia children in Lithuania as compared to the haemophilia children from more distant countries such as Egypt or Pakistan.

Another finding of the present study was that no significant differences were observed in dental health between adults with and without haemophilia. This was unexpected finding, particularly given that our adults with haemophilia had significantly higher dental plaque levels, reported greater consumption of soft drinks and noted more gum bleeding at rest or during tooth brushing as compared to their matched controls. Our findings are similar to the results obtained in Germany where it was found that oral health in patients with congenital coagulation disorders was not worse than the one observed in healthy subjects (34). While considering these findings, one must bear in mind the commonly encountered inherent limitation of case control studies when studying rare diseases. Such studies usually have relatively small sample sizes, thus these small numbers and inter-individual variations might hinder to find statisticaly significant differences despite that such differences may actually exist. In order to answer these important reserach question, multi-center studies might be necessary.

Relatively high proportions of both; adults (38.8%) and children (22.2%) with haemophilia reported dental pain being the reason for their last dental visit. Obviously, there is a need to increase the awareness among such patients about the importance of preventive and regular dental visits particularly among those for whom dental treatments have inherent health risks. Most importantly, timely dental visits may contribute to the

reduction of the prevalence of the two most common oral diseases among patients with haemophilia as well as among patients from the general population (14).

The importance of reducing the existing barriers in accessing primary dental care by patients with haemophilia cannot be underestimated. One possible way for the solution of this problem is to increase awareness and specific skills among practising dentists, both are necessary for the management of patients with bleeding disorders (13). It is also important to emphasize that the provision of operative dental treatments such as fillings, crowns or bridges or performing surgical treatments such as tooth extractions belongs to the secondary or tertiary prevention. Undoubtfuly, emphasizing the primary prevention which aims to reduce the need for invasive dental treatments will have a positive impact not only on the haemophilia patients but this may 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 to support more complex dental treatments (13).

Our results showed that 79.6% of adult haemophilia patients had gingivitis and this prevalence was significantly higher than the one observed in the control group. Our findings were consistent with the results reported in Italian, Turkish and Iranian studies (35–38). The amount of dental plaque is the most common reason of gingivitis and this emphasizes the importance of establishing good oral hygiene to prevent oral diseases as well as unnecessary bleedings in the haemophilia patients.

One of the aims of the present study was to examine and assess periodontal bone loss in haemophilia patients. We expected that haemophilia may be the aditional risk factor for periodontitis and subsequent alveolar bone loss. However, the results were unexpected: approximately 42.3% of the teeth of adult haemophilia patients had no alveolar bone loss and there were no significant differences in alveolar bone loss between the patients with and without haemophilia. It is known that chronic periodontitis mainly affects persons 35 years or older (39). The mean age of adults in our study groups was around 35 years, but it is likely that the life expectancy of haemophilia patients in the future may increase. Consequently we may observe higher prevalence of chronic periodontitis among the haemophilia patients in the future. Our findings differ from the findings of a similar study in German patients with congenital coagulation disorders

(CCD) (average age 39 years), which found statistically significant difference in alveolar bone loss between the CCD patients and healthy subjects (34).

Our study did not find statistically significant differences between the two study groups regarding the need for orthodontic treatments. We found that orthodontic treatment needs in the majority of the children with or without haemophilia (6–17 years) was moderate and our findings were comparable to other studies done in children from Lithuania, Latvia, Finland, Germany and Italy (40–44).

It is well known that oral health may influence people's physical as well as psychological well-being. Therefore, one of our aims was to examine oral health-related quality of life and compare patients with and without haemophilia. No statistically significant differences in the oral health-related quality of life between the study groups were found. The negative impact on the quality of life of haemophilia patients was assocaited with psychological discomfort and difficulties with food intake. Comparisons of the two adult study groups showed that the overal oral health-related quality of life was lower in the haemophilia patients as compared to their matched controls. However, these differences did not reach statistical significance; probably due to a small sample size and a relatively large inter-individual variation in the haemophilia group. In children, the most prominent differences were seen regarding the impact their diseases had on their family‘s life. Parents of children with haemopfilia were more concerned about the future of their children than parents of their matched controls. Unsurprisingly, children with haemophilia require more care and attention (45). Previous research has indicated that the quality of life of parents of haemophilia children is affected by the illness of their child, and that the parental quality of life mainly depends on the effectiveness of the haemophilia treatment and upon the difficulties experienced by their child (45, 46). Our findings in young adults are in contrast with the findings of a similar Turkish study (age 14–35 years), as we do not find significant differences between adults with and without haemophilia (47). However, the trends were similar when we compared our children with the Iranian study (age 2–15 years) (38). The differences among the studies may be due to variations in the provision of dental care in different countries. Therefore, future multi-center studies may be required to gain a better understanding of the haemophilia patients and how their disease impacts their general as well as oral health-related quality of life.

As it relates to the understanding of the risks or determinants of oral health-related outcomes (e.g. different aspects of oral health or disease) in a specific population, it is important to consider how evidence was acquired and a study‘s inherent limitations. Regarding the external validity of our findings, two main limitations need to be considered. Firstly, we had a relatively small sample size, thus the study was underpowered, consequently we could not reach statistically significance despite that we observed some obvious differences between the two study groups. To acquire a larger sample size was not feasible as all registered haemophilia patients in Lithuania were approached. Secondly, case control studies are recommended for studying rare diseases such as haemophilia, however this study design has inherent limitations not only not allowing causal inferences, but also this study design does not allow accurate control of confounders, potentially contributing to systematic bias (48). We tried to minimize the limitation of our study design by forming a control group from the same population. During our recruitment process we matched our cases with controls by age, gender and residency and due to these multiple matching aspects, we consider our findings to represent true trends of oral health related determinants in Lithuanian haemophilia patients.

An important study finding was that none of our multivariate models confirmed haemophilia to be an additional caries risk, i.e. seemingly Lithuanians with haemophilia do not have worse oral health than the general population. However, an important consideration is that dental treatments provided to haemophilia patients are substantially different from the treatments given to ordinary dental patients in that haemophiliacs not only have higher risks during the provision of dental treatments but they also need multiple visits to complete treatments even if on just one tooth (14). Consequently, maintaining oral health of patients with haemophilia should be a priority at least because of the risks inherent to the provision of dental treatments. Teaching how to manage the haemophilia patients should be included in the undergraduate as well as graduate dental curricula because of the inherent costs related to medical management of such patients and health risks; particularly encountered during extensive dental treatments. Concomitantly, it is important to increase professional awareness about the provision of safe dental treatments for such patients; which are possible due to innovations in the medical management of haemophilia patients (49). It is also important to acknowledge

that fear of dentists of haemophilia patients has unnecessarily contributed to the exaggeration of their actual risks experienced during dental treatments (50). Hematology should also be included in the curricula of undergraduate programme in dentistry (51). For example, a 10-year follow-up Italian study at three haemophilia centres demonstrated that by following the dental management protocol for the haemophilia patients dentists were able to provide safe and effective dental treatments with a low incidence of haemorrhagic and treatment-related complications even when dentists were providing extensive dental treatments (49).

Thus, it is important that dental care is easily accesible for this vulnerable group of patients, especially for those living at some distance from the regional centres. The aim should be to simplify dental care planning for this group of patients and dispel a number of the myths concerning their dental management (52). The benefits of primary oral health prevention aiming to preserve healthy teeth need to be repeatedly emphasized for patients with haemophilia and their dentists. Moreover, the prevention of oral diseases has a considerable cumulative cost-saving potential and also leads to a reduction of numbers of patients needing haemostatic treatments to control their haemophilia during the provision of more complex dental procedures (13). Consequently, dental management of patients with haemophilia and preventive dental care for them should be delivered as early as possible and reinforced at every dental visit, so that the need for advanced dental treatments could be minimized (33). Towards an overall improvement of oral health in this vulnerable segment of population, the integration of quality oral self-care into the everyday life of haemophilia treatment centers can be recommended, which should primarily aim towards the intensive prevention of oral diseases (53).

5. CONCLUSIONS

1. The prevalence of dental caries among Lithuanian children with haemophilia was 85.2% and among adults it was 100%. Overall caries experience and dental treatment needs for the deciduous dentitions were lower in the haemophilia children as compared to their counterparts without haemophilia. No significant differences between the study groups in either overall caries experience or dental treatment needs in the permanent dentitions were found.
2. There were also no statistically significant differences in oral hygiene between the children with and without haemophilia. Adults with haemophilia had significantly higher dental plaque levels and their gingiva status was significantly worse as compared to the control subjects.
3. Of all, 68.4% of children and adults with haemophilia had the need for the orthodontic treatments, but there were no significant differences between the study groups regarding such treatment needs either in the mixed or permanent dentitions.
4. Salivary levels of caries-associated bacteria such as *Streptococcus mutans* and *Lactobacilli* were lower in the children with haemophilia than in the control children. An overall caries experience in the deciduous dentition was statistically significantly associated with the increased salivary levels of *Streptococcus mutans* and *Lactobacilli*, lower salivary flow rate and low salivary buffering capacity. High levels of dental plaque and low buffering capacity of saliva were statistically significant predictors of the unmet dental treatment needs in the permanent dentition. Adults with haemophilia significantly more frequently consumed soft drinks as compared to their counterparts without heamophilia.
5. The impact of oral health-related quality of life was low in both study groups and there were no statistically significant differences between the haemophilia cases and their matched controls.

6. PRACTICAL RECOMMENDATIONS

1. We recommend to expand the content of the undergraduate dental program by training about the prevention of oral diseases and the specifically about the dental management of people suffering from systemic diseases, including haemophilia. Knowledge of dental practitioners should also be improved by educating them about the types of haemophilia, their severity levels, blood coagulation factors and algorithms of application of the missing coagulation factors. As a consequence, this training may contribute to assuring high quality, safe and efficient dental treatment services for haemophiliacs at the primary health care centers.
2. In order to reduce the prevalence of oral diseases of people with haemophilia, we recommended the integration of oral care with an individualized treatment plans and monitoring the oral health of haemophilia patients in the treatment centers. We encourage people with haemophilia to visit a dental practitioner on a regular basis and to advise general dental practitioners to engage their patients with haemophilia in the implementation of this plan.
3. To perform the education of people with haemophilia and their family members about the importance of oral health, prevention of oral diseases, and best preventative strategies. It is important not only to teach regular oral self-care, but also to demonstrate how to achieve optimal oral hygiene.
4. To focus on the oral care of people suffering from systemic diseases, including haemophilia in the national oral health program. To increase access for timely prevention and dental treatments for vulnerable adults and children from low socioeconomic status families, or people, who live further away from the major cities in Lithuania.

REFERENCES

1. Petersen PE, Ogawa H. Strengthening the prevention of periodontal disease: the WHO approach**.** *J Periodontol* 2005; 76:2187-93.
2. Monajam S. The WHO's action plan for oral health. *Int J Dent Hyg* 2009; **7**(1):71-3.
3. Petersen PE, Bourgeois D, Ogawa H, Estupinan-Day S, Ndiaye C. The global burden of oral diseases and risks to oral health. *Bull World Health Organ* 2005; 83:661–9.
4. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *Lancet* 2005; 19; 366(9499):1809-20.
5. Nibali L, Farias BC, Vajgel A, Tu YK, Donos N. Tooth loss in aggressive periodontitis: a systematic review. *J Dent Res* 2013; 92(10):868-75.
6. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, Ludlam CA, Mahlangu JN, Mulder K, Poon MC, Street A. Guidelines for the management of hemophilia. *Haemophilia* 2013; 19:1–47.
7. Mannucci PM, Tuddenham EGD. The hemophilias: from royal genes to gene therapy. *N Engl J Med* 2001; 344:1773–9.
8. Bolton-Maggs PH, Pasi KJ. Haemophilias A and B. *Lancet* 2003; 361:1801-9.
9. Gomez K, Bolton-Maggs PH. Factor XI deficiency. *Haemophilia* 2008; 14:1183-9.
10. White G, Rosendaal F, Aledort LM, Lusher JM, Rothschild C, Ingerslev J. Definitionsin hemophilia. Recommendation of the scientific subcommittee on factor VIII and factor IX of the scientific and standardization committee of the International Society onThrombosis and Haemostasis. *Thromb Haemost* 2001; 85:560.
11. De Moerloose P, Fischer K, Lambert T, Windyga J, Batorova A, Lavignelissalde G, Rocino A, Astermark J, Hermans C. Recommendations for assessment, monitoring and follow-up of patients with haemophilia. *Haemophilia* 2012; 18:319–25.
12. Fiske JP-FH, Savidge GF, Smith MP. The expressed dental needs of patients attending a Haemophilia Reference Centre. *J Disabil Oral Health* 2000; 1:20–5.
13. Kalsi H, Nanayakkara L, Pasi KJ, Bowles L, Hart DP. Access to primary dental care for patients with inherited bleeding disorders. *Haemophilia* 2012; 18:510-15.
14. Harrington B. Primary dental care of patients with haemophilia. *Haemophilia* 2000; 6(Suppl 1):7-12.
15. Azhar S, Yazdanie N, Muhammad N. Periodontal status and IOTN interventions among young hemophiliacs. *Haemophilia* 2006; 12:401–4.
16. 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.

17. Rossete MR, Rezende JS, Gomes VE, Ferreira E Ferreira, 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.
18. 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.
19. 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.
20. Aleksejuniene J, Scheie AA, Holst D. Inter-individual variation in the plaque formation rate of young individuals. *Int J Dent Hyg* 2006; 4:35–40.
21. 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.
22. Lahelma E, Martikainen P, Laaksonen M, Aittomaki A. Pathways between socioeconomic determinants of health. *J Epidemiol Community Health* 2004; 58(4): 327–32.
23. Lakhtin Yu. Comparative evaluation of periodontitis treatment of alpha lipoic acid at the short term and long term period. *Georgian Medical Ne*ws 2013; 218:19-22.
24. Walsh TF, Al-Hokail OS, Fosam EB. The relationship of bone loss observed on panoramic radiographs with clinical periodontal screening. *J Clin Periodontol* 1997; 24(3):153-7.
25. Brook PH, Shaw WC. The development of an index of orthodontic treatment priority. *Eur J Orthod* 1989; 11:309-20.
26. Slade GD, Spencer AJ. Development and evaluation of the Oral Health Impact Profile. *Community Dent Health* 1994; 11(1):3-11.
27. Jokovic A, Locker D, Stephens M, Kenny D, Tompson B, Guyatt G. Measuring parental perceptions of child oral health-related quality of life. *J Public Health Dent* 2003; 63:67-72.
28. Jokovic A, Locker D, Stephens M, Kenny D, Tompson B, Guyatt G. Validity and reliability of a questionnaire for measuring child oral-health-related quality of life. *J Dent Res* 2002; 81:459–63.
29. Jokovic A, Locker D, Tompson B, Guyatt G. Questionnaire for measuring oral health-related quality of life in eight- to ten-year-old children. *Pediatr Dent* 2004, 26:512–8.
30. Locker D, Jokovic A, Stephens M, Kenny D, Thomson B, Guyatt G. Family impact of child oral and oro-facial conditions. *Community Dent Oral Epidemiol* 2002; 30:438-48.

31. Kabil N, El Alfy M, Metwalli N. Evaluation of the oral health situation of a group of Egyptian haemophilic children and their re-evaluation following and oral hygiene and diet education programme. *Haemophilia* 2007; 13:287–92.
32. Mielnik-Blaszczak M. Evaluation of dentition status and oral hygiene in Polish children and adolescents with congenital hemorrhagic diatheses. *International Journal of Paediatric Dentistry* 1999; 9:99–103.
33. Boyd D, Kinirons M. Dental caries experience of children with haemophilia in Northern Ireland. *International Journal of Paediatric Dentistry* 1997; 7:149-53.
34. 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(3):527-31.
35. Ugolotti TG, Pizzi S, Tagliaferri A, Zini P. Dental, gingival and periodontal health indices in patients with inherited bleeding disorders. *Haemophilia* 2004; 10(Suppl 3):26-8.
36. Albayrak H, Ak G, Alpkilic E, Pynar A, Sepet E. Evaluation of oral and dental health in children with haemophilia. *Haemophilia* 2006; 12(Suppl 2):34-6.
37. Alpkilic Baskirt E, Albayrak H, Pinar Erdem A, Sepet E, Zulfikar B. Dental and Periodontal Health in Children with Hemophilia. *Journal of Coagulation Disorders* 2009; 1:7-10.
38. Salem K, Eshghi P. Dental health and oral health-related quality of life in children with congenital bleeding disorders. *Haemophilia* 2013; 19:65–70
39. Demmer R, Papapanou PN. Epidemiologic patterns of chronic and aggressive periodontitis. *Periodontology 2000* 2010; 53:28–44.
40. Baubiniene D,Sidlauskas A, Miseviciene I. The need for orhodontic treatment among 10-11- and 14-15-year-old Lithuanian schoolchildren. *Medicina* 2009; 45(10):814-21.
41. Liepa A, Urtane I, Richmond S, Dunstan F. Orthodontic treatment need in Latvia. *Eur J Ortho*d 2003; 25:279-84.
42. Väkiparta MK, Kerosuo HM, Nyström ME, Heikinheimo KAK. Orthodontic treatment need from eight to 12 years of age in an early treatment oriented public health care system: a prospective study. *The Angle Orthodontist* 2005; 75(3):334-49.
43. Tausche E, Luck O, Harzer W. Prevalence of malocclusions in the early mixed dentition and orthodontic treatment need. *The European Journal of Orthodontics* 2004; 26(3):237-44.
44. Perillo L, Masucci C, Ferro F, Apicella D, Baccetti T. Prevalence of orthodontic treatment need in southern Italian schoolchildren. *European Journal of Orthodontics* 2010; 32(1):49–53.

45. Beeton K, Neal D, Watson T, Lee CA. Parents of children with haemophilia- a transforming experience. *Haemophilia* 2007; 13(5):570-9.
46. Bullinger M, Von Mackensen S; Haemo-QoL Group. Quality of life in children and families with bleeding disorders. *J Pediatr Hematol Oncol* 2003; 25 (Suppl 1):S64-7.
47. Alpkilic Baskirt E, Ak G, Zulfikar B. Oral and general health related quality of life among young haemophilia patients. *Haemophilia* 2009; 15(1):193–8.
48. Schulz KF, Grimes DA. Case-control studies: research in reverse. *Lancet* 2002; 2 (359):431-4.
49. Franchini M, Rossetti G, Tagliaferri A, Pattacini C, Pozzoli D, Lorenz C, et al. Dental procedures in adult patients with hereditary bleeding disorders: 10 years experience in three Italian Hemophilia Centers. *Haemophilia* 2005; 11(5):504-9.
50. Zanon E, Martinelli F, Bacci C, Zerbinati P, Girolami A. Proposal of a standard approach to dental extraction in haemophilia patients. A case-control study with good results. *Haemophilia* 2000; 6(5):533-6.
51. Chuansumrit A. Treatment of haemophilia in the developing countries. *Haemophilia* 2003; 9:387-90.
52. 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.
53. Brewer AK. Advances in minor oral surgery in patients with congenital bleeding disorders. *Haemophilia* 2008; 14:119-21.

LIST OF PUBLICATIONS AND PRESENTATIONS

Publications from dissertation material

1. Zaliuniene R, Aleksejuniene J, Peciuliene V, Brukiene V. Dental health and disease in patients with haemophilia – a case-control study. *Haemophilia* 2014; 20(3): e194-e198.
2. Žaliūnienė R, Aleksejūnienė J, Brukienė V, Pečiulienė V. Do hemophiliacs have a higher risk for dental caries than the general population? *Medicina (Kaunas)* 2015; 51(1): 46-56.
3. Zaliuniene R, Peciuliene V, Brukiene V, Aleksejuniene J. Hemophilia and oral health. *Stomatologija, Baltic Dental and Maxillofacial Journal* 2014; 16: 127-131. Review.
4. Žaliūnienė R, Aleksejūnienė J, Brukienė V, Pečiulienė V. Oral health and its determinants in Lithuanian children with haemophilia. *Sveikatos mokslai* 2015; 25(1): 66-71.

Presentations from the dissertation material

1. Zaliuniene R, Peciuliene V, Aleksejuniene J, Brukiene V. Dental health and its determinants in Lithuanian haemophilia patients: a case control study. „31st World Congress of the World Federation of Haemophilia (WFH)“ 11-15th of May, 2014, Melbourne, Australia.
2. Zaliuniene R, Peciuliene V, Brukiene V, Puriene A, Rageliene L, Saulyte Trakymiene S, Gerbutavicius R, Malciute L, Gailiute N, Daubariene J. Educational project: building multi-professional network for haemophilia patients dental care access in Lithuania. Poster presentation „31st World Congress of the World Federation of Haemophilia (WFH)“ 11-15th of May, 2014, Melbourne, Australia.
3. Zaliuniene R, Peciuliene V, Brukiene V, Aleksejuniene J. Caries experience in children with haemophilia in Lithuania. Poster presentation „22nd Congress of the

International Association of Disability and Oral Health (IADH)“ 2-4th of October, 2014, Berlin, Germany.

4. Žaliūnienė R. Dental care for patient with haemophilia. „II Baltic haemophilia nurse symposium“ 11th of November, 2012, Vilnius, Lithuania.
5. Žaliūnienė R. Evaluation of the dental health situation of haemophilia patients in Lithuania. Scientific practical conference „Modern haemophilia treatment: achievements and challenges“ 7th of June, 2013, Kaunas, Lithuania.
6. Žaliūnienė R. Oral health in patients with haemophilia. Scientific conference “Relevant haemophilia treatment related issues”, 17 th of April, 2012, Birštonas, Lithuania.

ACKNOWLEDGEMENTS

I would like to extend my sincere gratitude to:

Prof. Dr. Vytautė Pečiulienė, DDs, PhD, MD, Head of Institute of Odontology Faculty of Medicine Vilnius University, my scientific consultant and supervisor of my PhD thesis. I would like to thank her for the encouragment and help in developing ideas, continuous professional and personal support.

Dr. Jolanta Aleksejūnienė, DDS, PhD, MD (The University of British Columbia) for the in-depth knowledge and valuable guidance in statistical analysis, interesting scientific discussions and overall consistent support.

Assoc. Prof. Dr. Vilma Brukienė, DDS, PhD, MD for her sincere assistance and support throughout the scientific research.

Professor Dr. Lina Ragelienė, DMS, PhD, MD for her patience, introduction and discussions of the unknown aspects in the field of hematology.

Also I would like to thank my collegues Dr. Deimantė Ivanauskaitė and Assoc. Prof. Dr. Laura Linkevičienė for their professional help and support in interpretation of radiological findings and evaluation of the needs for the orthodontic treatments.

And last but not least to my family for their warm support, patience and understanding.

CURRICULUM VITAE

R. Žaliūnienė was born in 1973, in Vilnius.

Educational background:

- Vilnius 56 th secondary school, Lithuania (1979 – 1990).
- Faculty of Stomatology, Kaunas Academy of Medicine, Lithuania (1991 – 1996); Diploma – Medical Doctor in Stomatology.
- Faculty of Stomatology, Kaunas Academy of Medicine, Lithuania (1996 – 1997); Internship Certificate – Dentist General Practitioner.
- Institute of Odontology, Faculty of Medicine, Vilnius University, Lithuania, postgraduate studies (2007 – 2010); Certificate – Specialist in Pediatric Dentistry.

Occupations:

- 2005 – 2010 a general dentist in the Hospital of Vilnius University, Žalgirio Clinic.
- 2010 to current, a pediatric dentist in the Hospital of Vilnius University, Žalgirio Clinic.
- 2012 to curent, an assistant in the Institute of Odontology, Faculty of Medicine, Vilnius University (Field: Pediatric dentistry).

SANTRAUKA

Įvadas

Burnos sveikata yra neatsiejama bendros žmogaus sveikatos dalis. Paskutiniojo dešimtmečio tyrimai rodo, kad burnos ligos išlieka globali visuomenės sveikatos problema tiek išsivysčiusiose, tiek besivystančiose šalyse: 2010 metais pasaulyje burnos ligomis sirgo 3,9 mlrd. žmonių, o šių ligų paplitimas per paskutiniuosius dvidešimt metų išaugo net 20,8 proc. (2, 3). Tokia situacija Lietuvoje ir pasaulyje skatina ieškoti kelių, kaip pagerinti burnos sveikatą. Svarbu nustatyti sisteminėmis ligomis sergančių pacientų burnos ligų paplitimą, nes tokių pacientų burnos ligų gydymas yra sudėtingesnis, brangesnis, kartais gali net kelti grėsmę pacientų gyvybei. Viena tokių pacientų grupė yra hemofilija sergantys asmenys.

Hemofilija – tai įgimta, su X chromosoma susijusi, recesyviniu būdu paveldima kraujo krešėjimo sistemos liga, siejama su VIII ir IX kraujo krešėjimo faktorių trūkumu. Ji vienodai paplitusi tarp skirtingų etninių, socialinių ir ekonominių grupių. Hemofilija serga tik vyrai, o moterys gali būti ligos nešiotojos. 2010 metų duomenimis, pasaulyje užregistruota 400 000 asmenų, sergančių įvairiomis hemofilijos formomis. 2011 metų duomenimis, Lietuvoje hemofilija diagnozuota 149 pacientams, beveik trečdalis jų yra vaikai.

Sergantieji hemofilija gali patirti gausų ir sunkiai stabdomą kraujavimą burnoje po danties pašalinimo, lūpos ar liežuvio pasaitėlių plastikos procedūrų, periodonto operacijų ar kitų chirurginių intervencijų. Tokiems pacientams net dantų valymasis ar kietesnio maisto kramtymas gali tapti dantenų kraujavimo priežastimi (12). Hemofilija sergantiems asmenims (HSA) tokie veiksniai, kaip nepakankama individuali ir profesionali burnos higiena bei laiku nepradėtas odontologinis gydymas, lemia ėduonies, gingivito, periodontito išsivystymą bei šių ligų komplikacijas. Tai tiesiogiai didina invazyvių odontologinio gydymo metodų naudojimo indikacijas ir apimtį bei kraujavimo tikimybę ir gali tapti sudėtinga, daugelio specialistų komandinio darbo reikalaujančia problema. Būtent todėl svarbiausias HSA burnos sveikatos užtikrinimo veiksnys turėtų būti savalaikė pirminė burnos ligų profilaktika (13).

Iki šiol hemofilija sergančių Lietuvos gyventojų burnos sveikatos būklė ir ją lemiantys veiksniai tirti nebuvo. Siekiant ištirti hemofilija sergančių Lietuvos gyventojų

burnos būklę, atlikti ją lemiančių veiksnių analizę, įvertinti burnos sveikatos nulemtą gyvenimo kokybę, užtikrinti reikiamos odontologinės pagalbos ir informacijos prieinamumą šia sistemine liga sergantiems asmenims bei suvienyti šiuos pacientus gydančių gydytojų pajėgas buvo pradėtas šis tyrimas.

Darbo tikslas – įvertinti Lietuvos gyventojų, sergančių hemofilija, burnos sveikatos būklę, gydymo reikmes ir burnos sveikatos nulemtą gyvenimo kokybę.

Darbo uždaviniai:

1. Ištirti ir įvertinti hemofilija sergančių asmenų dantų ėduonies paplitimą, intensyvumą ir gydymo reikmes.
2. Ištirti ir įvertinti hemofilija sergančių asmenų periodonto būklę.
3. Ištirti ir įvertinti hemofilija sergančių asmenų ortodontinio gydymo reikmes.
4. Įvertinti hemofilija sergančių asmenų burnos sveikatos būklę lemiančius veiksnius.
5. Įvertinti hemofilija sergančių asmenų burnos sveikatos nulemtą gyvenimo kokybę.

Medžiaga ir metodai

Tyrimui atlikti buvo gautas Vilniaus regioninio biomedicininių tyrimų etikos komiteto leidimas (2011-11-08; Nr. 158200-11-425-119). Tyrime kviesti dalyvauti visi Lietuvoje gyvenantys ir hemofilija sergantys asmenys nuo 4 metų amžiaus; suformuota kontrolės asmenų grupė, kurioje asmenys atitiko tiriamuosius pagal lytį, amžių ir gyvenamąją vietą. Atliekant tyrimą remtasi Pasaulinės sveikatos organizacijos rekomendacijomis burnos sveikatos tyrimams atlikti. Kiekvienam tyrime dalyvaujančiam asmeniui buvo atlikti skatinto seilėtekio, buferinės gebos ir bakteriologiniai seilių tyrimai, apskaičiuotos dantų ėduonies intensyvumo (KPI/kp), gydymo reikmių, gydymo patirties, dantų sveikatos, ortodontinio gydymo reikmių (IOTN), papilos, kraštinių, prisitvirtinusių dantenų (PMA) ir kiekybinio apnašų indeksų reikšmės. Viršūninio ir kraštinio periodonto būklei vertinti buvo atliktas rentgeninis pacientų tyrimas. Siekiant išsiaiškinti veiksnius, lemiančius hemofilija sergančių asmenų

burnos sveikatą, atlikta tiriamųjų apklausa. Burnos sveikatos nulemta gyvenimo kokybė tirta apklausos būdu naudojant suaugusiųjų burnos sveikatos nulemtos gyvenimo kokybės (OHIP-14) ir vaiko burnos sveikatos nulemtos gyvenimo kokybės (COHQoL) klausimynus.

Rezultatai

Tyrime dalyvavo 155 asmenys: 76 hemofilija sergantys asmenys ir 79 kontrolės grupės nariai. Visų tiriamųjų amžiaus vidurkis – 26,1 metai (SN±14,4), hemofilijos atvejų grupės amžiaus vidurkis 26 metai (SN±14,3), kontrolės grupės – 26,3 metai (SN±14,6). Hemofilija A buvo diagnozuota 65 atvejų grupės pacientams (85,5 proc.), o hemofilija B – 11 pacientų (14,5 proc.).

Dantų ėduonies paplitimas hemofilijos atvejų grupėje siekė 94,7 proc., kontrolės grupėje – 96,2 proc. Nustatytas dantų ėduonies paplitimas skirtingais amžiaus periodais: hemofilija sergančių vaikų (4–17 metų) ėduonies paplitimas siekė 85,2 proc., hemofilija sergančių suaugusiųjų (18–60 metų) – 100 proc., kontrolės grupės vaikų – 93,3 proc., kontrolės grupės suaugusiųjų – 97,9 proc.

Palyginus hemofilija sergančių ir kontrolės grupės vaikų pieninių dantų ėduonies intensyvumą (kp) nustatyta, kad ėduonies pažeistų ir plombuotų pieninių dantų skaičius tarp šių grupių statistiškai reikšmingai skyrėsi (p=0,003): hemofilijos atvejų grupėje ėduonies intensyvumas buvo mažesnis (2,6±2,6) negu kontrolės grupėje (6,1±2,5). Statistiškai reikšmingas skirtumas (p=0,036) gautas palyginus hemofilija sergančių ir kontrolės grupių vaikų pieninių dantų gydymo reikmes (kd): hemofilija sergančių vaikų pieninių dantų gydymo reikmės (1,4±1,9) buvo mažesnės negu kontrolės grupės vaikų (3,6±2,9). Palyginus nuolatinių dantų ėduonies intensyvumą (KPI) tarp atvejų (9,4±7,6) ir kontrolės (9,3±7,0) grupių, statistiškai reikšmingo skirtumo negauta (p=0,947). Panašūs rezultatai gauti ir palyginus nuolatinių dantų gydymo reikmių, gydymo patirties ir dantų sveikatos indeksų reikšmes: atvejų ir kontrolės grupių duomenys statistiškai nesiskyrė (p>0,05). Hemofilija sergantys vaikai turėjo statistiškai reikšmingai mažesnį dantų ėduonį sukeliančių bakterijų (*Streptococcus mutans* ir *Lactobacilli*) kiekį seilėse (p=0,019), statistiškai reikšmingai rečiau (p=0,005) naudojo higieninį dantų siūlą ir buvo iš žemesnės socialinės ir ekonominės padėties šeimų (p=0,004) negu kontrolės grupės

vaikai. Suaugusiųjų grupėje burnos sveikatą lemiančių rizikos veiksnių analizė parodė, kad hemofilija sergančių suaugusiųjų dantų apnašų kiekis buvo statistiškai reikšmingai didesnis (p=0,014), jų dantenos statistiškai reikšmingai dažniau kraujavo ramybės metu (p=0,014), jie statistiškai reikšmingai rečiau (p=0,014) naudojo higieninį dantų siūlą ir dažniau vartojo saldintus, gazuotus gėrimus (p=0,025) negu to paties amžiaus ir gyvenamosios vietos kontrolės grupės asmenys.

Daugialypės tiesinės regresijos modeliai parodė statistiškai reikšmingą ryšį tarp pieninių dantų ėduonies intensyvumo (Santykis.kp) ir ėduonį sukeliančių bakterijų (*Streptococcus mutans* ir *Lactobacilli*) kolonijų tankio seilėse (β=0,548, p=0,005), seilių tekėjimo greičio (β=0,492, p=0,004) ir buferinės seilių gebos (β=0,414, p=0,017). Analizuojant nuolatinių dantų gydymo reikmes statistiškai reikšmingi veiksniai buvo dantų apnašos (β=0,330, p<0,001) ir žema buferinė seilių geba (β=0,251, p=0,002).

Pagal IOTN ortodontinio gydymo reikmių indekso dantų sveikatos komponento reikšmes nustatyta, kad 31,6 proc. hemofilija sergančių asmenų (4–60 metų) ortodontinio gydymo nereikėjo, o 68,4 proc. buvo reikalingas įvairios apimties ortodontinis gydymas. Palyginus hemofilijos atvejų ir kontrolės grupių ortodontinio gydymo reikmes mišraus ir nuolatinio sąkandžių periodais statistiškai reikšmingo skirtumo nebuvo (p>0,05).

Statistiškai reikšmingai skyrėsi hemofilijos atvejų ir kontrolės grupių suaugusiųjų kraštinių dantenų būklė (p=0,002) ir prisitvirtinusių dantenų būklė (p=0,001): hemofilija sergančių suaugusiųjų dantenų būklė buvo blogesnė negu kontrolės grupės asmenų. Vertinant dantenų būklę pagal šešias dantų grupes statistiškai reikšmingi skirtumai tarp tiriamųjų grupių gauti viršutinio žandikaulio abiejų pusių galinių dantų (p=0,004) bei apatinio žandikaulio dešinės (p=0,006) ir kairės (p=0,007) pusių galinių dantų dantenų spenelio srityje; viršutinio ir apatinio žandikaulių abiejų pusių galinių dantų ir apatinio žandikaulio priekinių dantų kraštinių dantenų srityje (p<0,05); abiejų žandikaulių dešinės pusės galinių dantų grupėse (p=0,010; p=0,030) bei priekinių dantų grupėse (p=0,049; p=0,003) prisitvirtinusių dantenų srityje.

33,8 proc. (n=24) hemofilijos atvejų ir 44,7 proc. (n=34) kontrolės grupių tiriamųjų panoraminėse rentgeno nuotraukose buvo nustatyti radiologiniai viršūninio periodonto patologijos požymiai, tačiau statistiškai reikšmingo skirtumo tarp grupių nebuvo gauta (p=0,141). Analizuojant panoraminių rentgeno nuotraukų atvaizdus buvo

mezialiai ir distaliai įvertinta visų tiriamųjų nuo 18 metų (n=98) kiekvieno burnoje esančio danties (n=2476) (išskyrus trečiuosius krūminius dantis) kraštinio periodonto būklė. 42,3 proc. hemofilija sergančių suaugusiųjų tirtų dantų kraštinis kaulas buvo be patologijos požymių.

Atlikus suaugusiųjų burnos sveikatos poveikio bendrai gyvenimo kokybei dažnių analizę pagal atskiras OHIP-14 klausimyno dalis matyti, kad didesnis procentas abiejų grupių tiriamųjų neturėjo gyvenimo kokybę bloginančių burnos sveikatos simptomų. Palyginus hemofilijos atvejų ir kontrolės grupių suaugusiųjų burnos sveikatos nulemtą gyvenimo kokybę statistiškai reikšmingų skirtumų nenustatyta (p=0,240). Statistiškai reikšmingų skirtumų negauta ir lyginant hemofilija sergančių ir kontrolės grupių vaikų burnos sveikatos nulemtą gyvenimo kokybę (p>0,05), bet vaiko dantų ir burnos sveikata hemofilija sergančių vaikų tėvams turėjo didesnį poveikį (3,1±3,5) negu kontrolės grupės vaikų tėvams (2,0±1,9).

Išvados

1. Dantų ėduonies paplitimas tarp hemofilija sergančių vaikų siekė 85,2 proc., o tarp suaugusiųjų – 100 proc. Hemofilija sergančių vaikų pieninių dantų ėduonies intensyvumas ir gydymo reikmės buvo reikšmingai mažesnės negu bendraamžių kontrolės grupės vaikų. Nuolatinių dantų ėduonies intensyvumas ir gydymo reikmės tarp hemofilija sergančiųjų ir kontrolės grupių statistiškai reikšmingai nesiskyrė.
2. Hemofilija sergančių ir kontrolės grupės vaikų burnos higienos būklė reikšmingai nesiskyrė. Suaugusiųjų vidutinis dantų apnašų kiekis buvo statistiškai reikšmingai didesnis, o dantenų būklė reikšmingai blogesnė hemofilijos grupėje.
3. Ortodontinis gydymas buvo reikalingas 68,4 proc. hemofilija sergančių vaikų ir suaugusiųjų. Hemofilijos atvejų ir kontrolės grupių asmenų ortodontinio gydymo reikmės mišraus ir nuolatinio sąkandžių periodais nesiskyrė.
4. Hemofilija sergantys vaikai turėjo reikšmingai mažesnį *Streptococcus mutans* ir *Lactobacilli* bakterijų kolonijų tankį seilėse negu kontrolės grupės vaikai. Pieninių dantų ėduonies intensyvumas buvo statistiškai reikšmingai susietas su padidėjusiu *Streptococcus mutans* ir *Lactobacilli* bakterijų kolonijų tankiu seilėse,

sumažėjusiu seilių tekėjimo greičiu ir žema buferine seilių geba. Reikšmingi nuolatinių dantų gydymo reikmių veiksniai buvo didelis dantų apnašų kiekis ir žema buferinė seilių geba. Hemofilija sergantys suaugusieji gazuotus ir saldintus gėrimus vartojo reikšmingai dažniau negu kontrolės grupės asmenys.

5. Burnos sveikatos poveikis hemofilija sergančiųjų bendrai gyvenimo kokybei buvo mažas. Hemofilija sergančių ir kontrolės grupės asmenų burnos sveikatos nulemta gyvenimo kokybė reikšmingai nesiskyrė.