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ORIGINAL ARTICLE

Oral health in predialysis patients with emphasis on diabetic nephropathy

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Abstract We investigated oral health of chronic kidney disease (CKD) patients at predialysis state. The hypothesis was that diabetic nephropathy affects oral health more detrimentally than other CKD patients due to the known risk diabetes presents in this regard. We expected worse oral health and particularly poor periodontal health among the diabetic patients. A cross-sectional study was conducted in the Helsinki University Central Hospital, Finland, on 148 patients with different kinds of kidney disease at predialysis state. Data from medical records, clinical oral examination, saliva, and mucosal yeast counts were analyzed and compared between the disease groups. Of the patients, 53 (36%) had diabetic nephropathy (29 patients with type 1, 24 patients with type 2 diabetes). Compared with other CKD patients, diabetic patients had poor glycemic control as expected (mean HbA_{1C} 8.0% vs 5.9%, $p<0.01$). Diabetic patients also had more dental caries (mean number of carious teeth 5.1 vs 3.1, $p<0.01$) and lower salivary flow rates than other CKD patients (stimulated salivary flow 1.2 ml/min vs 1.6 ml/min, $p<0.05$). No difference between groups was observed in periodontal health and yeast counts. In conclusion, diabetic nephropathy patients indeed had worse dental health in comparison to CKD group. However, contrary to our expectation, diabetic nephropathy did not seem to affect periodontal health more severely than the other kidney diseases.

Keywords Oral health · Predialysis · Kidney disease · Diabetes · Nephropathy

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Introduction

The prevalence of chronic kidney diseases (CKD) is increasing worldwide [1]. Diabetes remains one of the leading causes of CKD, and the prevalence of diabetes of all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030; the total number of diabetic patients is projected to rise globally from 171 million in 2000 to 366 million in 2030 [2]. Other important etiologies of CKD are hypertension, chronic glomerulonephritis (CGN), and systemic autoimmune diseases [3]. Furthermore, atherosclerotic renovascular disease, polycystic kidney disease (PKD), obstructive uropathy, and chronic pyelonephritis may also cause CKD [3, 4].

Diabetes is a well-known risk factor also for periodontal disease. For example, Mealey [5] concluded that diabetic patients had a threefold higher risk of periodontal disease compared with nondiabetic patients after controlling for age, sex, and other confounding factors. Periodontal disease also appears to be more severe in patients with diabetes [6, 7]. For example, studies on Pima Indians in Arizona showed that loss of periodontal attachment and bone loss were greater in diabetic vs nondiabetic individuals within different age groups [8]. Thorman et al. [9] showed that uremia patients have more dental problems than healthy

controls. Uremia patients had significantly worse dental status regarding to decayed, missing, and filled teeth (DMFT) index, periodontal loss of attachment, and periapical lesions. The patients seem to develop their problems before they have progressed to dialysis. Therefore, greater attention to dental problems may be warranted during the progression of uremia. However, a recent study by Llambés et al. [10] investigating the effect of periodontal treatment on the metabolic control of diabetes did not find any effect on HbA_{1C} values 3 months after treatment. Hence, the issue remains controversial.

Consequently, we became interested in studying whether diabetic nephropathy reflects in oral health differently when compared with other CKDs. Our study hypothesis was that diabetic nephropathy patients present worse oral health than patients with other CKDs. We hereby describe results from an open cross-sectional study conducted on predialysis state patients. The study presented here is the first part of a longitudinal investigation on CKD patients who are being followed from predialysis state up to posttransplant state. To our knowledge, there are no previous reports where aspects of oral health would have been examined in predialysis stage of CKD.

Materials and methods

The patients

The study was conducted at the Divisions of Nephrology and Oral and Maxillofacial Diseases of the Helsinki University Central Hospital (HUCH), Helsinki, Finland. The hospital is a tertiary referral center with catchment area of 1.4 million inhabitants living in the Helsinki metropolitan area. All predialysis phase (for definition, see below) patients from this area are referred to our hospital where they are further referred for oral and dental examination. In the present study, altogether, 178 subsequent patients with CKD were examined during the years 2000–2005. The exclusion criteria were based on Ethical Committee of the Helsinki and Uusimaa Hospital District (see below), and therefore, no children, pregnant or breastfeeding women, handicapped, or prisoners were included in this study. Thirty patients were excluded because their GFR (assessed by 24-h creatinine clearance) was higher than 20 ml/min/1.73 m^2. The remaining 148 patients (99 men and 49 women, aged 23–83 years) with glomerular filtration rate (GFR)$\leq$20 ml/min/1.73 m^2 were finally included in our study. This inclusion criterion corresponds the mid of CKD stages 4 (defined by GFR$<$30 ml/min/1.73 m^2) and 5 (GFR$<$ 15 ml/min/1.73 m^2) and is in our department the definition for predialysis phase. Patients with GFR below this threshold value are evaluated for dialysis and renal transplantation. The threshold values are generally accepted nephrological criteria.

Of the patients included, 53 (36%) had diabetic nephropathy (29 patients with diabetes type 1 and 24 patients with diabetes type 2), 29 (20%) had CGN, 32 (22%) had PKD, and 19 (13%) had other specified kidney disease; 15 patients (10%) had unspecified renal failure. The diagnosis of diabetic nephropathy was based either on (a) histological findings in renal biopsy or (b) verified diabetes with concomitant retinopathy associated with proteinuric renal disease. Medical records of all patients were available, and blood samples were taken in the hospital and analyzed using routine methods.

The protocol had been approved by the Ethical Committee of the Helsinki and Uusimaa Hospital District

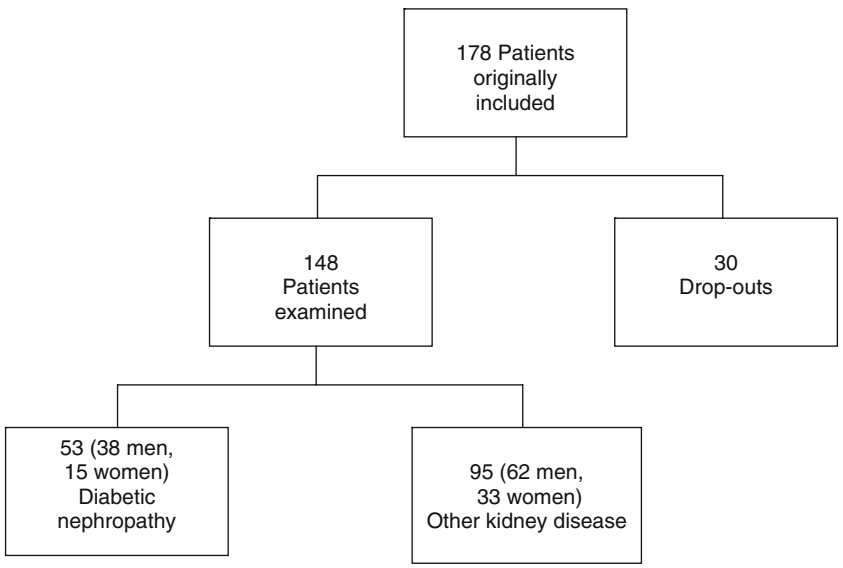

Fig. 1 Study profile

(HUS99/E6/2000). The study was registered in the HUCH database for clinical trials (www.hus.fi). All participants gave informed consent to take part in this study. The patients are presented in more detail in Fig. 1 and Table 1.

Table 1 Characteristics of the study groups (percentage and number of patients)

	Diabetic nephropathy, *N*=53	Other kidney disease, *N*=95
Sex (M/F)	38/15	61/34
Age (±SD)	52 (±13.6)	54 (±12.8)
Smoking, % (*n*)	55% (28)	45% (39)
Concomitant diseases, % (*n*)		
Cardiovascular	62% (33)	51% (48)
Respiratory	8% (4)	6% (6)
Gastrointestinal	4% (2)	11% (10)
Urological	43% (23)	11% (10)
Orthopedic	0% (0)	2% (2)
Psychiatric	4% (2)	4% (4)
Neurological	30% (16)	6% (6)
Endocrinological	9% (5)	21% (20)
Dermatological	0% (0)	0% (0)
Hematological	2% (1)	3% (3)
Cancer	6% (3)	3% (3)
Ophthalmological	45% (24)	0% (0)
Otorhinological	0% (0)	0% (0)
Rheumatic	9% (5)	8% (8)
Number of drugs used daily per patient	10±2.3	8±3.1*
Medication		
Antibiotics and antimicrobial drugs	4% (2)	6% (6)
Cardiovascular drugs	100% (53)	99% (94)
Respiratory drugs	6% (3)	3% (3)
Gastrointestinal and urological drugs	25% (13)	12% (11)
Sex hormones and gynecological drugs	2% (1)	5% (5)
Psychiatric drugs	13% (7)	18% (17)
Neurological drugs	6% (3)	6% (6)
Drugs for allergy	0% (0)	0% (0)
Endocrinological drugs	100% (53)	79% (75)
Dermatological drugs	0% (0)	0% (0)
Analgesics and antirheumatic drugs	9% (5)	6% (6)
Electrolytes	21% (11)	34% (32)
Hematological and oncological drugs	62% (33)	58% (55)
Ophthalmological drugs	2% (1)	1% (1)
Otorhinological drugs	0% (0)	0% (0)
Vitamins	98% (52)	96% (91)

*$p<0.05$

Clinical oral examination, yeast counts, and salivary flow rate analyses

Clinical oral examination took place in a normally equipped dental unit of the hospital. All the patients were examined by the same periodontist (HR). World Health Organization (WHO) criteria were used in recording the oral health status [11]. The DMFT index was calculated. The number of teeth with dental erosion was recorded (recorded yes/no based on clinical evaluation). The number of periodontal pockets after probing with a WHO periodontal probe was recorded. Periodontal treatment need was assessed using the WHO community periodontal index of treatment needs [12]. Panoramic radiographs of the jaws were taken and analyzed by hospital radiologist specialized in dental and oral radiology. Particular attention was paid to eventual signs of dental infection. Mucosal health was also recorded using the WHO criteria for oral mucosal pathology [13].

Cotton swabs were used to sample cheek mucosa and dorsal surface of the tongue for detection of yeasts. The Transpocult® dip-slide method was used for cultivation (*Orion Diagnostica, Espoo*, *Finland*). Resting saliva was collected for 5 min using the free-flow method according to Meurman and Rantonen [14]. Stimulated saliva samples were also collected for 5 min by giving the patients a standard piece (1 g) of paraffin wax to chew, and the chewing rate was approximately once per second. Saliva samples were collected at least an hour after previous meal and/or smoking and always in the afternoon to avoid diurnal variation. Salivary flow rate was measured as milliliter per minute.

Statistical analyses

Data were analyzed between patients with diabetic nephropathy and other CKD patients. *T* test was used for parameters normally distributed while binomial data were analyzed with cross tabulations and chi-square test.

Results

Table 2 gives the results of blood analyses of the patients. As expected, the HbA_{1C} values of the diabetic patients were significantly higher than those in the other disease groups. No difference was observed between the groups in the other background variables analyzed in this respect. However, the diabetic nephropathy patients also took statistically significantly more drugs daily than the other kidney disease groups ($p<0.05$).

Table 3 gives the oral health characteristics of the groups. There were no totally edentulous subjects among

Table 2 Biochemical profile and protein concentration in urine of the patients (means with SD)

	Diabetic nephropathy	Other kidney disease	Significance
Hemoglobin (g/l)	114 (14.48)	117 (12.42)	NS
Hematocrit (%)	34 (483)	35 (3.99)	NS
Leukocytes (×E09/l)	7.2 (1.69)	6.6 (2.17)	NS
Thrombocytes (×E09/l)	263 (84.88)	225 (69.17)	NS
Potassium (mmol/l)	4.3 (0.53)	4.6 (0.60)	NS
Sodium (mmol/l)	139 (4.56)	139 (3.67)	NS
Ionized calcium (mmol/l)	1.16 (0.10)	1.19 (0.10)	NS
Phosphate (mmol/l)	1.51 (0.34)	1.65 (0.46)	NS
Creatinine (μmol/l)	457 (126.42)	530 (158.91)	NS
Albumin (g/l)	34 (5.47)	36 (4.29)	NS
Intact parathormone (ng/l)[a]	218 (161.71)	257 (265.65)	NS
Creatine clearance (ml/min)	14.4 (4.8)	13.8 (4.2)	NS
Glycosylated hemoglobin (%)	8.0 (1.68)	5.9 (1.21)	*
Urea (mmol/l)	24.4 (6.43)	24.3 (7.82)	NS
Urinary protein (mg/24 h)	3,529 (674)	2,965 (539)	NS

NS not significant

[a] Reference values 8–73 ng/L

*$p<0.01$

Table 3 Oral health findings

	Diabetic nephropathy	Other kidney disease	Significance
Mean no. of teeth with SD	21.5±7.2	22.9±8.3	NS
No. (and %) of patients with partial dentures	12 (22.6%)	23 (25%)	NS
No. (and %) of patients with dental caries	52 (98%)	79 (83%)	*
Mean no. of carious teeth with SD	5.1±4.6	3.1±3.33	*
No. (and %) of patients with			NS
Gingivitis	7 (13%)	18 (19%)	
4–5 mm periodontal pockets	22 (42%)	43 (45%)	
>5-mm pockets	23 (45%)	33 (34%)	
No. (and %) of patients with dental erosion	10 (19%)	10 (11%)	NS
Findings on oral mucosa (no. and % of patients)[a]			NS
Healthy	40 (76%)	79 (83%)	
Hyperplasia	11	12	
Denture stomatitis	2	5	
Hairy tongue	1	0	
Erythroplakia	1	0	
Lichen planus	1	0	
Leukoplakia	0	1	
No. (and %) of patients with positive yeast count	19 (36%)	22 (23%)	NS

NS not significant

[a] Three patients in the diabetic nephropathy group and two patients in the other kidney disease group had more than one mucosal pathology

*$p<0.01$

the patients. Most patients in both study groups had untreated dental caries, but the prevalence was significantly higher among the diabetic nephropathy patients regarding both the percentage of patients with carious teeth ($p<0.01$) and the number of carious teeth per patient ($p<0.01$). No statistically significant difference was observed in the periodontal health markers. Nevertheless, the number of patients with deep periodontal pockets was high; 45% in the diabetic and 34% in the other kidney disease groups, respectively. In the mean, the number of >5-mm-deep periodontal pockets per patient was four in both groups with a range from 1 to 19.

Dental erosion was detected more often, but not significantly, in the diabetic nephropathy patients than in the other kidney disease group. There was no difference in the prevalence of oral mucosal pathology between the groups. Gingival hyperplasia was the mucosal lesion most often encountered in both groups. Yeast counts were more often positive in the diabetic than other kidney disease group, but the difference was not statistically significant. The yeasts detected were of the species *Candida albicans* in most cases (70%). In addition, *Geotrichum candidum*, *Candida tropicalis*, and *Aspergillus* were found in individual cases. In general, yeasts were detected in 58% of the patients who had dentures in the diabetic nephropathy group, and *C. albicans* were the species found in 42% of these patients. In the other CKD group, only 30% of the denture patients had positive yeast count. *C. albicans* was found in 17% of these cases.

Resting salivary flow rate values were 0.4±0.9 ml/min in the diabetic group, 0.2±0.7 ml/min in the CKD patients (n.s.). Mean stimulated salivary flow rate was significantly lower in the diabetic nephropathy group: 1.2±0.4 ml/min vs 1.6±0.5 ml/min, respectively ($p<0.05$).

Discussion

The results showed that patients with diabetic nephropathy had worse dental health than patients with other kidney diseases in the predialysis state. Our study hypothesis was thus partly confirmed. A putative reason for the finding of poor dental health is the lower stimulated salivary secretion rate observed in the diabetic nephropathy group when compared with the other CKD group. Reduced salivary flow is a well-known risk for dental health. The patients with diabetic nephropathy also used statistically significantly more drugs than the other CKD patients. Närhi et al. [15] have shown that the more drugs a patient takes daily, the greater is the effect on salivary secretion irrespective of the nature of medication. In our patients, practically all needed cardiovascular medicines known to affect saliva secretion [16]. Nevertheless, the fact that the diabetic nephropathy group presented more often reduced salivary flow rates may be partly due to the diabetes itself. This disease is known to cause reduced saliva secretion and dry mouth [17, 18]. Studies by Karjalainen et al. [19] and Miralles et al. [20] have reported an association between dental caries and the HbA_{1C} level. This was indeed poor among our diabetic nephropathy patients.

A number of patients had deep periodontal pockets, 45% and 34% in the diabetic vs other kidney disease groups, respectively, indicating periodontitis. However, this difference was not statistically significant, and the result was thus contrary to our expectation. Diabetes, especially when poorly controlled, increases the risk of periodontitis [21]. Periodontal disease may predict the development of nephropathy and end-stage renal disease with type 2 diabetic patients [22]. The diabetic patients had indeed statistically significantly higher HbA_{1C} values indicating poor metabolic control as could be expected.

We observed positive yeast counts in 36% and 23% of the diabetic vs CKD groups, respectively. Several authors have reported that diabetic patients have an increased predisposition to manifestations of oral candidiasis which, in turn, associates with poor glycemic control and use of dentures [23, 24]. Having dentures linked distinctly with positive yeast counts in both patient groups also in the present study. The diabetic nephropathy patients might be more liable to yeast infections in this regard since 58% of them vs 30% of the other CKD patients with dentures had yeasts. However, we observed no difference between the groups in the prevalence of mucosal lesions which could be partly linked with oral yeast infections.

The present study was the first comprehensive investigation of oral health and salivary flow rates in patients suffering from different types of predialysis stage kidney diseases. However, we need to emphasize that this was an open cross-sectional study, and hence, controlled follow-up studies are needed for further conclusions. Furthermore, due to study design, there are no data about the patients' earlier behavioral and other possibly confounding issues which may weaken the validity of the present results. Nevertheless, based on the current results, it seems warranted to carefully observe dental caries status and salivary flow rates of predialysis patients with diabetic nephropathy in particular. All CKD patients should be advised in preventive dental therapy.

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Conflict of interests The authors declare that they have no conflict of interest.

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