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Oral findings and periodontal status in children, adolescents and young adults suffering from renal failure

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Abstract

Aim: Describe the oral condition of chronic renal failure and healthy subjects, and the relationship between oral variables, chronic renal failure (CRF) conditions, and their treatment.

Materials and Methods: Four renal failure groups: chronic renal disease ($n = 22$); undergoing dialysis ($n = 22$); after dialysis and transplant ($n = 21$); and after transplant ($n = 32$), and a healthy control ($n = 38$) were examined. Caries, enamel hypoplasia, pulp obliteration, plaque index, gingival bleeding, recession, overgrowth and index, probing depths, attachment loss, renal treatments and their relations with the oral variables were analysed.

Results: The renal failure groups had higher gingival index (GI) and bleeding, probing depths, attachment loss, hypoplasia and obliteration and less caries, than the control. Plaque was higher in the dialysis and pre-dialysis (PD) groups. Overgrowth was evident after transplant. The PD group showed lower GI than other renal groups. Dialysis duration and end-stage renal failure significantly correlated with gingivitis, probing depth, attachment loss and enamel hypoplasia. Immuran® correlated positively with probing depth, gingival recession and attachment loss. Normiten® and Nifedipine® had positive correlations with gingival overgrowth.

Conclusions: CRF patients are characterized by pulp obliteration, gingival and periodontal diseases. Duration of end stage renal failure and type of systemic treatment have a significant influence on the oral condition.

Key words: oral disease; renal failure

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The incidence of chronic renal failure (CRF) and end-stage renal failure (ESRF) is constantly rising since parenchymal cure is rare (Goh et al. 1994, Berthoux et al. 1999). The end-result of a reduced renal glomerular filtration (GFR) is uraemia, which is a metabolic state or intoxication affecting many organs including the heart, lungs, brain and intestines, as well as the endocrine function; additional systemic conditions related to renal failure include hypertension, anemia and bone disease (renal osteodystrophy) (McKay et al. 1996, Schrier & Gottschalk 1997, Davidovich & Sinai-Treiman 1998, Fogo & Kon 2004). Renal replacement therapy (RRT) and treatments such as haemo- and peritoneal dialysis have improved considerably; however, they will still leave the patient with $\leqslant 20\%$ of normal renal function (McKay et al. 1996, Schrier & Gottschalk 1997, Davidovich & Sinai-Treiman 1998, Fogo & Kon 2004). After transplantation of a kidney, renal function can return to borderline normal values. However, it often decreases in the course of a longtime follow-up.

All CRF/ESRF patients, but mostly those after renal transplantation, are prescribed numerous medicines that have significant multi-organ side effects (McKay et al. 1996, Schrier & Gottschalk 1997, Davidovich & Sinai-Treiman 1998, Fogo & Kon 2004). Due to the universal lack of sufficient organs for renal transplantation (RTx) it is expected that the total number of patients living in a moderate to severe uraemic state will increase exponentially, including children. Similarly for the complications of the basic renal disease and its treatment.

CRF and ESRF in children treated conservatively or with RRT, have special features not seen in adults such as severe growth impairment, which can be treated with growth hormone, as well as delayed physical, sexual and mental/psychological maturation, requiring the attention of a multidisciplinary team. (McKay et al. 1996, Schrier & Gottschalk 1997, Davidovich & Sinai-Treiman 1998, Fogo & Kon 2004).

The increasing number of children and adolescents with CRF, and their successful treatment is of significant interest to the dental profession since CRF and ESRF and their treatment may cause numerous oral disturbances such as: pallidness of the oral mucosa, uraemic stomatitis, petechiae and ecchymoses (Kho et al. 1999); gingival inflammation (Wolff et al. 1985, Gavalda et al. 1999, Kitsou et al. 2000); gingival overgrowth (Slavin & Taylor 1987; Thomason et al. 1993, Karpinia et al. 1996, Wilson et al. 1998, Nunn et al. 2000), loss of attachment (Tollefsen & Johansen 1985a, Tollefsen & Johansen 1985b, Naugle et al. 1998, Kitsou et al. 2000, Ganibegovic 2000), enamel hypoplasia. (Bublitz et al. 1981, Wolff et al. 1985, Koch et al. 1999, Nunn et al. 2000) and pulp obliteration (Nasstrom et al. 1985, Galili et al. 1991, Ganibegovic 2000). On the other hand, a low prevalence of dental caries is observed in these patients, since the metabolic end products of bacterial plaque are neutralized by increased pH resulting from urea hydrolyzation in the saliva. (Wolff et al. 1985, Naugle et al. 1998, Kho et al. 1999, Nunn et al. 2000).

Most studies on the oral manifestations associated with CRF and ESRF have been performed on groups of $\leqslant 45$ patients, focused mainly in adults after a kidney transplant, and without addressing the relation between the oral and systemic parameters, and there is no study comparing the oral findings in relation to CRF severity and its treatment modalities. Therefore, the aim of the present study is to describe in a relatively large population of children, adolescents and young adults suffering from CRF, their prevalence and severity oral diseases, and their relation to type, duration and severity of the renal disease, and their treatment modalities.

Materials and Methods

After approval by the Institution Review Board for research on human subjects and informed consent, 97 subjects were randomly selected from a population of patients receiving treatment in Pediatric Nephrology departments of two hospitals in Israel. The CRF group included: 54 patients (55.7%) from the Schneider Hospital and 43 (43.3%) from the Sharei Zedeck Hospital: 67 males (69.1%) and 30 females (30.9%). None of the patients had diabetes. A control group (C group, $n = 38$) who had no systemic disease, received treatment in a regular dental clinic, and matched the CRF population in age and gender, was also included in the study. According to the Schwartz scale (Schwartz et al. 1976), the CRF patients were divided as follows: (a) with renal disease with no previous dialysis, or pre-dialysis (PD group, $n = 22$); (b) under dialysis (D group, $n = 22$); (c) after dialysis and transplant (DT group, $n = 21$) and (d) with a transplant without previous dialysis (T group, $n = 32$) (Table 1).

All the exams were done by one author. However, before recording the clinical data, the examiner (E.D.) and another author (Z.S.), who is a specialist in Periodontology, calibrated the clinical examination. The examiner could not be blind to the subject's general systemic condition, since they were either examined in a hospital or in a regular clinic. On the other hand the examiner was ''blind'' to the subgroup of renal failure.

Evaluation of clinical oral variables was performed at the buccal and lingual surfaces of the maxillary: right first permanent molar or the right primary second molar; the primary or permanent left central incisor; the right first bicuspid or primary molar; and the mandibular: left first permanent molar or second primary molar; right central primary or permanent incisor; right first bicuspid or first primary molar. It included: (a) Plaque index (PI) (Löe & Silness 1963); (b) Gingival index (GI) (Silness & Löe 1964); (c) Number of sites with bleeding on probing (BOP); (d) Probing depth – the distance from the free gingiva to the bottom of the gingival sulcus using a Wiliams probe; (e) Recession – the distance from marginal gingival to the cemento-enamel junction (CEJ) also using a Wiliams' probe; (f) Clinical attachment loss (AL) – calculated as the sum of recession and probing depth and (g) Gingival overgrowth – distance >2 mm from the gingival margin to the CEJ using a Wiliams' probe. In addition, the presence and severity of enamel hypoplasia (Ainamo & Cutress 1982, Clarkson & O'Mullane 1989) was classified according to the most severe hypoplasia found at any tooth by the following scale: 1, no hypoplasia; 2, horizontal white discoloration, no missing enamel; 3, horizontal yellow-brown discoloration, no missing enamel (hypomaturazion); 4, pitted; 5, horizontal fissures; 6, stained whole enamel; 7, whole hypoplastic enamel; 8, morphologic anomalities. The number of decayed, missing and filled carious surfaces in the primary and permanent teeth was also recorded.

Radiographs were selected based on the following criteria: (a) none to minimal distortion of radiographic image due to inadequate angulation of the radiographic machine and/or radiograph bends; (b) none to minimal overlapping between proximal tooth surfaces; (c) possibility for measuring the distance from the CEJ to the alveolar bone (AB) in the mesial and distal surfaces

Table 1. Distribution of patients by group, gender and age

	Group				
	Pre-dialysis (PD) (GFR $<30^*$)	Dialysis (D) (complete renal failure)	Transplanted + previous dialysis (DT) ($40<$GFR$<80^*$)	Transplanted (T) ($40<$GFR$<80^*$)	Control (C) (normal renal function)
Number of subjects	22	22	21	32	38
Female	4	8	7	11	23
Male	18	14	14	21	15
Age (mean ± SE)	10.0 ± 0.57	14.3 ± 1.11	14.9 ± 1.54	15.6 ± 1.13	12.6 ± 1.04

*Glomerular renal filtration.

of all teeth. Radiographs were obtained from all patients, but only 61 out of the 97 individuals with CRF and all the control individuals had radiographs that fit the required criteria. The selected radiographs were examined by the examiner (E.D.) and another author (E.B.) independently for periodontal disease and obliteration; in cases of disagreement the radiographs were examined by both authors together and an agreed diagnosis was recorded. Radiographic evaluation of obliteration and alveolar bone loss was done by examining bite wings and a maxillary anterior periapical radiograph.

Alveolar bone loss (ABL) was recorded when the distance from the cemento-enamel junction to the alveolar bone (CEJ-AB) was >2 mm and there was complete loss of lamina dura over the alveolar bone (Greenstein et al. 1981, Aass et al. 1994, Bimstein 1995). Obliteration was recorded only when clear evidence of abnormal mesio-distal narrowing of the pulp cavity was evident, and was considered partial (a narrow pulp cavity still evident) or complete (no pulp cavity evident), and if located only in the crown or in the crown and root.

The systemic condition of the patients was evaluated by the following systemic variables: (a) renal function, reflected as the GFR and creatinine serum levels in patients not in dialysis, according to Schwartz formula (Schwartz et al. 1976); (b) bone status by clinical (bone deformities) and/or radiographic signs (osteopenia, rickets, subperiostal resorption) and (c) laboratory findings: (haemoglobin, serum calcium (Ca), serum phosphorous (P), serum alkaline phophatase (AlP), serum parathyroid hormone (PTH), serum albumin, and serum 1, 25 $(OH)_2D3$. The type and dosage of medicaments prescribed to each patient were recorded. The patients or the patients and their parents, were informed on the oral treatment needs and were offered the possibility to receive comprehensive oral treatment. Regarding the medications, dosages/kg body weight were taken into account, except to the medications: tacrolimus and cyclosporine in which both dosages/kg body weight and blood levels were taken into account.

Statistical analysis

For the statistical analysis utilized a standard statistical computer program (JMP, version 5, 1989–2002, SAS Institute Inc., Cary, NC, USA) and included an analysis of variance (ANOVA) to examine the significance of the differences between the oral parameters in the different groups. When a difference was found, a Tukey–Kramer analysis for multiple regression analysis was utilized to elucidate what groups were statistically different from the others. The Pearson correlation analysis was utilized to examine the significance of the correlation between oral variables and between the oral and systemic variables. χ^2 analysis was utilized to examine the significance of the differences in means and distribution of categorical variables. A $p = 0.05$ level of significance was chosen. Multiple regression analysis was utilized to find the statistical significance of the relation of each variable on gingival inflammation when controlling for other variables that also correlated significantly with gingival inflammation, in the CRF groups.

Results

The mean age for the different groups is presented in Table 1; it ranged from 2 to 27 years in the CRF group (mean = 13.9, SE = 0.67), and from 3 to 29 years in the control group (mean = 12.6, SE = 1.2). The serum values of the individuals with CRF are presented in Table 2. As expected, high levels of phosphorus were found in the PD group (5.63+0.23). In group D, the PTH levels were increased (208.02+22.89), whereas haemoglobin values were low (10.53+0.29) as compared to the other CRF patients.

Analysis of the differences in oral variables values between the different CRF groups (Table 3) indicated: no significant differences between the CRF groups in bleeding on probing, probing depths and clinical attachment loss; PI was significantly higher in groups D and PD when compared to group C; group D had significantly higher plaque scores, compared to groups DT and T; group PD showed a significantly lower GI compared to the other patients although it was still statistically significantly higher than group C; gingival overgrowth (Figs 1 and 2) was significantly increased in the groups DT and T as compared to all other groups, a slight increase in gingival growth was also found in the PD and D groups Group C had statically higher DMFS than all the other groups; severity of enamel hypoplasia (Fig. 2) was signifi-

Table 2. Laboratory data (mean ± standard error) in the CRF subgroups

	Pre-dialysis (PD) $N = 22$	Dialysis (D) $N = 22$	Transplanted (T) $N = 32$	Dialysis +transplant (DT) $N = 21$	ANOVA*
Creatinine	1.85+0.61	Non-relevant	1.98+0.51	1.68+0.63	$p = 0.02$
GFR	16.69+6.26	Non-relevant	42.79+3.91	48.02+4.55	$p = 0.0001$
Ca	9.36 ± 0.12†	9.73 ± 012†	9.84 ± 0.1	10.0 ± 0.12‡,§	$p = 0.01$
P	5.63 ± 0.23†,¶	4.81 ± 0.23	4.01 ± 0.2‡	3.95 ± 0.23‡	$p = 0.0001$
PTH	121.28 ± 23.45§	208.02 ± 22.8¶,‡,†	55.8 ± 19.48§	94.86 ± 22.36§	$p = 0.0004$
Alkaline phosphatase	208.19 ± 20.63	193.04 ± 20.63	151.31 ± 17.56	147.06 ± 20.16	$p = 0.01$
Albumin	4.15 ± 0.06	3.83 ± 0.06	4.12 ± 0.05	4.35 ± 0.06	$p = 0.001$
Hemoglobin	11.42 ± 0.29§	10.57 ± 0.29¶,‡,†	11.69 ± 0.24§	11.59 ± 0.29§	NS

*Analysis of variance.

†Statistical difference from group DT.

‡Statistical difference from group PD.

§Statistical difference from group D.

¶Statistical difference from group T.

Statistical difference between groups analyzed by Tukey–Kramer analysis, $p \leqslant 0.05$.

CRF, chronic renal failure; GFR, glomerular renal filtration; PTH, parathyroid hormone.

Table 3. Oral variables values (mean ± standard deviation) by group

	Control (C) $N = 38$	Pre-dialytic (PD) $N = 22$	Dialysis (D) $N = 22$	Transplanted (T) $N = 32$	Dialysis+transplant (DT) $N = 21$
Plaque index	1.09 ± 0.08	1.45 ± 0.11*	1.56 ± 0.10†,‡,*	1.38 ± 0.09§	1.08 ± 0.10§
Gingival index	0.38 ± 0.09	1.70 ± 0.12*,†,‡	2.17 ± 0.12¶,*	2.14 ± 0.09*,¶	2.11 ± 0.12*
Bleeding on probing	0.92 ± 0.30	3.91 ± 0.39*	4.687 ± 0.39*	4.21 ± 0.33*	4.09 ± 0.40*
Probing depth	1.49 ± 0.09	2.07 ± 0.11*	2.24 ± 0.11*	2.13 ± 1.09*	2.12 ± 0.12*
Recession	0.14 ± 0.07	0.06 ± 0.09	0.25+0.09	0.19 ± 0.07	0.24 ± 0.09
Clinical attachment loss	1.35 ± 0.10	1.75 ± 0.13*	1.97 ± 0.13*	1.85 ± 0.10*	1.77+0.13*
Gingival over growth	0.00 ± 0.03‡,†	0.08 ± 0.05‡,†	0.08 ± 0.05‡,†	0.16 ± 0.04*,¶,§	0.3 ± 0.05*,¶,§
#carious surfaces	0.25 ± 0.02	0.01 ± 0.02*	0.02 ± 0.02*	0.01 ± 0.01*	0.00 ± 0.02*
Hypoplasia	0.00 ± 0.25	3.41 ± 0.34*	4.31 ± 0.34*	4.21 ± 0.28*	4.04 ± 0.35*

*Statistical difference from group C.
†Statistical difference from group T.
‡Statistical difference from group DT.
§Statistical difference from group D.
¶Statistical difference from group PD.
Statistical difference between groups analyzed by Tukey–Kramer analysis, $p \leqslant 0.05$.

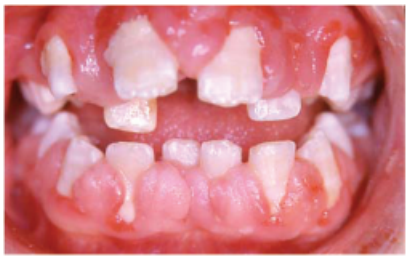

Fig. 1. Clinical picture of a patient after kidney transplant. Note the gingival overgrowth and inflammation.

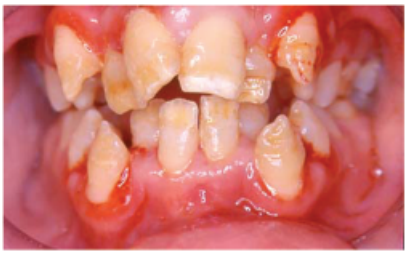

Fig. 2. Clinical picture of a patient after kidney transplant. Note the gingival overgrowth and inflammation and the enamel hypoplasia.

cantly lower in group C. In the control as well as in the CRF groups, there were significant positive correlation between the patients' average for PI and: the patient average for probing depths ($r = 0.41$ and $p = 0.009$ and $r = 0.41$, $p = 0.0000$ respectively); GI ($r = 0.51$, $p = 0.0001$ and $r = 0.40$, 0.0000 respectively); and number of bleeding sites ($r = 0.35$, $p = 0.03$ and $r = 0.47$, $p = 0.000$ respectively). PI significantly correlated with the patients' average of attachment loss only in the CRF group ($r = 0.38$, $p = 0.0001$). Gingival inflammation correlated significantly with: age in the CRF and in the control groups ($r = 45$, $p = 0.0000$ and $r = 0.35$, $p = 0.03$ respectively); PI in the CRF and the control groups ($r = 0.40$, $p = 0.0000$ and $r = 0.57$, $p = 0.03$ respectively). In CRF and the control groups, plaque still had a significant effect on gingival inflammation when controlling for age ($p = 0.001$ for both), and age had a significant effect on gingival inflammation when controlling for plaque ($p = 0.001$ and $p = 0.01$ respectively).

Pulp obliteration (Fig. 3) was absent in the group C, and present in the 4 CRF groups (Table 4). Complete obliteration was more common than partial obliteration (54.1% and 42.6% respectively), and present in most of the individuals in groups D (76.9%) and DT (68.7%), whereas most of the children in groups PD (81.8%) and T (52.4%) had partial obliteration (Chi square, $p = 0.0001$). The incidence of caries was found to be higher in females than in males in the CRF groups (mean = 0.02, SE = 0.005 and mean = 0.007, SE = 0.003 respectively).

Renal osteodystrophy was found in 30 patients, alveolar bone loss present in only 12 of the individuals with renal osteodystrophy; in five females and seven males: five each in the D and DT groups, and seven in group T. Alveolar bone loss was not evident in group C. No statistical analysis was done in relation to alveolar bone loss and renal osteodystrophy due to their low prevalence.

Correlation between oral parameters and duration of chronic renal failure were examined only in the PD and D groups since in most transplanted patients, there is deterioration of kidney functioning, after a period of normal graft function, and it is difficult to estimate the duration of renal failure. Duration of dialysis and end stage renal failure had a positive significant correlation with GI, probing depth and attachment loss. Dialysis duration also correlated with increase in PI, bleeding sites, gingival growth, gingival recession, and enamel hypoplasia. The length of CRF correlated significantly with the degree of hypoplasia ($r = 0.49$, $p = 0.01$) in the PD group, and with PI ($r = 0.53$, $p = 0.009$) and gingival recession ($r = 0.59$, $p = 0.003$) in the D group.

Examination of the significance of the correlations between the oral variables and the hematologic values, indicated significant correlations between: (a) alkaline phosphatase and PI ($r = 0.2$, $p = 0.04$), and gingival recession ($r = -0.21$, $p = 0.03$); (b) phosphorous values and GI ($r = -0.19$, $p = 0.04$), and attachment loss ($r = -0.19$, $9 = 0.05$); (c) haemoglobin and GI ($r = 0.26$, $p = 0.008$) and (d) number of bleeding sites and albumin ($r = 0.20$, $p = 0.04$). Analysis of the significance of the correlation between the gingival variables and medications indicated statistical significant correlations between: (1) Immuran® (Generics, UK; immunosuppressive agent, lymphocyte proliferation inhibitor) and probing depth ($r = 0.43$, $p = 0.001$), gingival recession ($r = 0.37$, $p = 0.05$), and attachment loss ($r = 0.36$, $p = 0.006$) and (2) Normiten® (Teva Pharmaceuticals Ind. Ltd., Nethanya, Israel; anti-hypertensive, β blocker) and Nifedipine® (ABIC Ltd., Nethanya, Israel; anti-hypertensive, calcium channel blocker) with gingival overgrowth ($r = 0.28$, $p = 0.004$ and $r = 0.22$, $p = 0.02$ respectively). ANOVA of the gingival

overgrowth values for the individuals receiving different medicament regimens indicated a statistically significant difference among values for the different groups: Tacrolimus® (Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan; immunosuppressive agent) only ($n = 14$, mean = 0.22, SE = 0.09); Cyclosporine® (Sandoz Pharmaceuticals, AG, Switzerland; immunosuppressive agent) only ($n = 16$, mean 0.24, SE = 0.08); Tacrolimus® and Nifedipine® ($n = 13$, mean = 0.36, SE = 0.09); Cyclosporine® and Nifedipine® ($n = 6$, mean = 0.47, SE = 0.14).

Discussion

The present study provides evidence of periodontal disease with significantly higher attachment loss, recessions and probing depths in CRF patients when compared to a healthy cohort. The progression of periodontal disease was correlated with bad oral hygiene, the patient's uraemic status, and the duration of renal disease. Interestingly, in the PD and D groups there was an explicit correlation between periodontal disease progress and duration of end stage renal failure and dialysis, indicating progression of periodontal disease. Duration of dialysis indicated the extent period of end stage renal failure; the most severe kidney's damage with all the derived complications. To the best of our knowledge, our study is the first to show the relationship between the duration of dialysis and periodontal disease in children. This phenomenon corresponds to other body systems (renal osteodysthrophy, anaemia, growth disturbance etc.), that reach to their greatest insult at the time of end stage renal failure and worsen during dialysis.

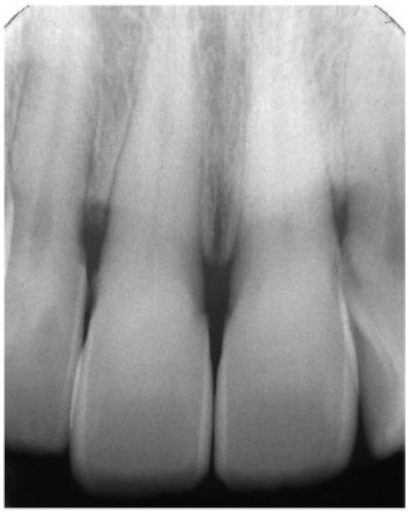

Fig. 3. Periapical radiograph of the anterior maxillary teeth of a patient with renal failure. Note the obliteration of the pulp chambers and root canals.

A previous study (Hugoson et al. 1981) indicates that in children and adolescents the highest prevalence of gingivitis is found in the lingual surfaces of the lower molars and the buccal surfaces of the upper molars Therefore, we limited our clinical examination to these teeth, however, we examined the lingual and buccal surfaces of the teeth. Poor oral hygiene was found in the present study in pre-dialysis patients and patients undergoing dialysis, this finding confirms previous reports (Wolff et al. 1985, Klassen & Krasko 2002). This finding may be related to the existence of chronic disease, and its influence on the lifestyle and prolonged hospitalizations.

In the CRF patients, gingival inflammation had a significant positive correlation with age, PI and sulcus depths, and was significantly higher than in the control group. In addition, it became evident that in the CRF group the gingival response to plaque was stronger than in the control group when controlling for age. The subject of gingival inflammation in CRF patients appears to be controversial in the literature; while some reports indicate reduced gingivitis in these patients (Tollefsen et al. 1982, Tollefsen & Johansen 1985a, b, Nunn et al. 2000), due to immunosuppression and uraemia that may inhibit gingival reaction to plaque stimulation, others indicate opposite findings (Wolff et al. 1985, Naugle et al. 1998). Furthermore, Kitsou et al. (2000) were able to induce experimental gingivitis in CRF patients and concluded that chronic uraemia has no effect on the defence of periodontal tissue against microbial plaque. In the present study, gingival and periodontal variables significantly correlated with the duration of CRF and dialysis sugesting that immunosuppression state and uraemia in transplanted and dialysis patients may reduce, but does not eliminate, the inflammatory response of the gingiva and periodontium to plaque.

Bleeding on probing was examined separately to GI because of coagulation disturbances in CRF patients (impaired thrombocyte function and heparin administration during dialysis in transplanted patients). No information on bleeding on probing in CRF patients was found in the literature. In the present study, bleeding sites prevalence was significantly higher in the CRF groups as compared to the controls who had normal coagulation (the dialysis group showing the highest gingival bleeding prevalence). This finding may be related to more severe gingival inflammation and/or coagulation disturbances in CRF patients. However, one should take in consideration that the examination was performed 1 h after dialysis. Therefore, the patients were heparinized and the urea reduction was not enough to improve thrombocytes function).

In adults with no systemic disease, periodontal pockets correlate directly with age (Newman et al. 1994), oral hygiene (Axelsson et al. 2004), and gingival inflammation (Trombelli & Tatakis 2003). In the present study, a direct correlation between periodontal

Table 4. Distribution of dental pulp obliteration in the control and the CRF groups

	Control		Pre-dialysis		Dialysis		Transplanted		Dialysis and transplant		Total for CFR	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
None	38	100	0	0.0	1	7.7	0	0.0	1	6.3	2	3.3
Partial	0	0.0	11	81.8	2	14.4	9	52.4	4	25.0	26	46.6
Complete	0	0.0	10	18.2	10	76.9	2	47.6	11	68.7	33	54.1
Total	38	0.0	21	100	13	100	11	100	16	100	61	100

Statistically significant difference in the distribution by groups, χ^2, $p = 0.0001$. CRF, chronic renal failure.

pockets and oral hygiene and gingival inflammation was observed. However the finding that periodontal pockets were significantly deeper in the CRF groups than in the control indicates a different mechanism of periodontal disease in CRF patients. Furthermore, the significant correlation between periodontal pockets and the duration of renal failure suggests that prolonged renal dysfunction has a direct effect on the progression of periodontal disease.

Previous studies indicate higher incidence of attachment loss in CRF patients compared to healthy subjects (Naugle et al. 1998, Kitsou et al. 2000, Ganibegovic 2000). Our study further supports these findings, and reveals a higher incidence of attachment loss in the CRF subjects than in the control group. Among the CRF groups, the most severe attachment loss was found in group D. Furthermore, attachment loss correlated with the duration of dialysis and end stage renal failure. These findings suggest that attachment loss may be influenced by the uraemic status and its duration.

There are few studies in the literature on alveolar bone loss as part of renal osteodysthrophy (ROD). Previous findings include absence of lamina dura, loss of borders of mandibular canal, ground glass appearance and deviations in trabecular pattern of the bone (Wolff et al. 1985, Ganibegovic 2000). Yet, in another study (Frankenthal et al. 2002) no correlation was found between haemodialysis therapy and secondary hyperparathyroidism. In the present study, 12 patients had alveolar bone loss while systemic bone disease was found in 30 subjects. These findings should be carefully considered since bone disease is a prolonged process with varying severity which depends on the severity of renal failure, its treatment, and patients' compliance. Therefore, estimation at a specific time cannot define this complex and prolonged process. In addition, it may be possible that the damage to the alveolar bone develops at later stages, when the damage to other parts of skeleton is already outstanding.

Gingival overgrowth is a well known phenomenon that has been related to local factors (plaque accumulation) as well as a side effect from the administration of drugs such as Diphenylhydantoin, Cyclosporine A and Verapamil (Moghadam & Gier 1995). Our findings confirm that gingival overgrowth is common in patients after organ transplantation, and that gingival overgrowth in patients treated with tacrolimus is less prevalent and milder than in patients treated with cyclosporine (Slavin & Taylor 1987, Thomason et al. 1993, Karpinia et al. 1996, Wilson et al. 1998, Nunn et al. 2000). Extensive gingival overgrowth was found in transplanted patients due to the use of Cyclosporin, and most likely also related to calcium channel blockers and poor oral hygiene in the pre-dialytic and dialysis patients. The positive significant correlation between the length of dialysis and gingival overgrowth may also be related to prolonged calcium channel blocker administration. Enhancement of gingival overgrowth due to cyclosporine or tacrolimus by additional nifedipine administration is probably a result of additive effect (Slavin & Taylor 1987). Interesting is that no correlation between dosage or blood levels of neither tacrolimus nor cyclosporine to gingival overgrowth were found; this may be the result of a strong influence of other factors that also influence gingival overgrowth such as plaque accumulation and drug pharmacokinetics.

Few reports describe pulp obliteration, or pulp narrowing due to tissue calcification, related to renal diseases (Nasstrom et al. 1985, Galili et al. 1991, Ganibegovic 2000). The present study indicates a significantly higher percentage of CRF patients with pulp narrowing than in the control. The direct correlation between pulp obliteration and duration of renal failure and dialysis suggests that pulp obliteration is related to disturbances in calcification processes, due to parathyroid disturbances and administration of calcium containing phosphate binders (Caltrate®) in CRF patients. In fact, there is more recently reported evidence on calcifications in other systems related to administration of calcium containing phosphate binders in these patients.

Our findings confirm that there is a low incidence of caries in CRF patients (Wolff et al. 1985, Naugle et al. 1998, Kho et al. 1999, Nunn et al. 2000). The finding might be explained by the fact that high amounts of urea in the saliva can lead to an increase in its buffering ability as a result of high concentration of ammonia arising from urea hydrolyzation. Enamel hypoplasia is a well known phenomenom in CRF patients (Bublitz et al. 1981, Wolff et al. 1985, Koch et al. 1999, Nunn et al. 2000). Accordingly, in the present study, enamel hypolasia was significantly more extensive and more severe in patients with CRF than in the control group. Interesting is the present finding that enamel hypoplasia was evident in the deciduous dentition, indicating the possibility of a congenital disease, as previously described by Koch et al. (1999). The severity of hypoplasia correlated with age, and the duration of end stage renal failure and dialysis suggesting that CRF may influence dental morphogenesis. The fact that some oral variables did not significantly correlate with some of the examined laboratory parameters is not surprising, since laboratory examination at a specific time cannot reveal oral disturbances, which are expression of a prolonged process of renal failure, its severity and treatment.

Many medications are prescribed to the CRF and ESRF patients depending on the patient condition and renal function. The major groups of medication include immunosuppressive drugs, steroids, calcineurin inhibitors, lymphocyte proliferation inhibitors, antihypertehsive drugs and others such as resprim, aspirin, bicarbonate, caltrate vitamin D and growth hormone. Interestingly, we found that Immuran® correlated with increased attachment loss, gingival pockets and gingival overgrowth. This findings may indicate that inhibition of T cytotoxic cells by Immuran® enhances the progression of periodontal disease.

A prominent finding in our study was the direct correlation between the duration of dialysis and chronic renal failure and periodontal parameters indicating correlation with the existence and progression of periodontal disease. This may be an additional argument for the need of transplantation without any dialysis treatment in children and young adults. Dentists should keep in mind that the establishment and progression of most oral diseases can be controlled. Therefore, oral examination and treatments should be an integral part of the complex multi-disciplinary treatment of CRF patients.

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Clinical Relevance

Scientific rationale for the study: Dentists should be aware of distinctive oral characteristics related to individuals with renal failure (RF) and its treatment.

Principal findings: RF and its treatments have been found, in previous and the present study, to significantly affect the dental, gingival and periodontal tissues. In addition we found that these effects relate to the duration of the end stage renal failure, the diverse CRF stages and treatments.

Practical implications: The present findings may help the clinician to diagnose prevent and treat oral diseases in individuals with renal failure.