COMPARATIVE ANALYSIS OF PERIODONTAL STATUS IN HEMODYALYSIS PATIENTS – A CLINICAL APPROACH

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ABSTRACT

Introduction. Both periodontal disease and chronic kidney disease (CKD) are inflammatory disorders that considerably affect the patients' overall health and life quality. Periodontal disease occurs somehow more often in CKD people, but it remains indeterminate whether periodontal disease is an independent risk factor in this population or what the true nature of their relationship is. **Objectives.** Our study focused on investigating the relationship between CKD and periodontitis, and the influence of the latter's presence and severity on the former, through evaluation of the periodontal status in predialysis and dialysis CKD and healthy subjects with periodontitis. **Materials and method.** The patients included in our study were divided in two groups, study (n=59) with end-stage CKD and periodontitis, and control (n=20), with periodontitis but without renal impairment. All the subjects underwent dental and periodontal evaluation, using parameters common in clinical examination (Periodontal Disease Index –PDI, dental mobility, bleeding on probing – BOP, inflammatory hyperplasia, gingival recession, probing depth – PD and clinical attachment loss – CAL). Both groups also answered questions about their meal plan and oral hygiene habits and their access to dental care. **Results.** There were visible differences between the groups when considering social and economic status and access to dental and periodontal services, which is relevant for the distribution of periodontal disease severity between groups (56% from the study group had severe periodontitis, with only 10% in the control group). The study group also had more missing teeth, deeper periodontal pockets and more signs of inflammation. It is still unclear if this is due only to low social and economic status or is it a consequence of CKD and hemodialysis. **Conclusions.** There is a link between the two entities, but it is still unclear if this is due just to the pathophysiology of periodontitis and CKD, or are the external and local factors involved. Further investigation is needed to clarify this issue and to be able to produce viable prevention and treatment programs for people with end-stage CKD.

Keywords: *periodontal disease, end stage CKD, hemodialysis*

INTRODUCTION

Periodontal disease (PD) is defined, according to the 1999 American Association of Periodontology (AAP) Consensus as "a bacterially induced, localized, chronic inflammatory disease, destroyed connective

tissue and bone that support the teeth" (Consensus Report: Chronic Periodontitis, 1999). The incidence of PD in western countries' population varies, reaching 35% for chronic forms (Hugoson et al., 2008) and 10% for severe forms (Burgeois et al., 2007).

The mechanism of PD is complex and still unclear. If initially, the bacterial factor was considered the main culprit in pathogenesis, directly destroying the host tissues (Haffajee, Socransky, 2005), now it is considered that the host-associated factors, such as genetic factors, oxidative stress and the immune-inflammatory response (Kinane, Lappin, 2002, Albu et al., 2012) and environment factors – diet, smoking, stress, health status and sociodemographic elements, contribute greatly to the initiation and progress of this disorder (Hasturk, Kantarci, 2015). Recent studies (Marsh et al., 2011) have demonstrated that the pathogenic biofilm represent in fact an increase of commensal bacteria and the induction of inflammatory pathways by them is essential for the appearance of inflammation in the periodontium.

Inflammation in periodontitis appears at the same time the bacterial products penetrate the junctional and crevicular epithelium, which determines the accumulation of neutrophils in the tissues. Periodontal status becomes chronic when the microbial species continue to grow and can't be eliminated by the acute reaction or when there is a deficient immune response, which leads in turn to the extension of the inflammatory status.

Chronic disease is the main cause of death in the world, based on WHO reports, which indicate that from the total of 56.888.289 deaths in the year 2008, 36.121.871 were due to chronic illness (Yeun et al., 2000). Chronic kidney disease (CKD) as an entity, is a subject that goes beyond the area of nephrology, involving a complex approach through evolution associated with cardiovascular and cerebrovascular disease and, thus, being considered a public health issue on a world scale. Recent data concerning CKD epidemiology in Romania indicates that 10.500 adults have CKD (Cepoi et al., 2012).

Identifying CKD risk patients and those in early (1-2) stages, without significant kidney involvement, is possible through basic laboratory tests, with lower costs compared to those needed for kidney replacement therapy, when the disease is already present and in development. Moreover, time efficient treatment has real chances of preventing or delaying complications determined by low kidney function, delaying the progression of disease and reducing the risk of cardiovascular events mediated through several oxidative mediators (Filip et al., 2017; Levey et al., 2007).

It was thought initially, that inflammation in end stage CKD is connected to various clinical comorbidities (Grodstein et al., 1980), but further studies have shown that an inflammatory syndrome may be found in the absence of any clinically visible inflammatory disease (Kaysen et al., 2000) – a so-called „micro inflammation" or „occult inflammation". Occult inflammatory episodes may be recurrent (Kaysen, 2000) or persistent, determining an „acute phase chronic reaction" (Kalantar-Zadeh et al., 1998). This chronic inflammation status may be secondary to factors such as: chronic subclinical infections, the absorption of intestinal bacteria or from the dialysis solution endotoxins, the accumulation of advanced glycation end-products and impaired oxidative status, cardiac insufficiency, or dialysis systems bio incompatibility (Albu et al., 2013;

Stenvinkel, 2001).

Studies that investigate the relationship between periodontal disease and CKD are few, with inconclusive results. For example, Chambrone has identified 2456 eligible studies, out of which, 4 were cross-sectional, one retrospective and 3 interventional (Chambrone et al, 2013). A different study has reviewed data bases, identifying 88 studies in 125 populations (11.340 adults) (Ruospo et al, 2014). Moderate or severe periodontal disease is associated with a high risk or cardiovascular death in the general population and, also, in CKD patients and it is likely that inflammation may be the key factor which explains this relationship.

OBJECTIVES

Based on the evidence that proves the prevalence of periodontal disease in the general population and, although their relationship with other diseases, such as cardiovascular disease or diabetes mellitus is highly debated, this research was focused on investigating the correlations between CKD and the presence and severity of periodontal disease (PD). Our study was an observational, longitudinal one, with a comparative analysis of periodontal status in predialysis or dialysis CKD patients and subjects with periodontitis, but without kidney disease.

MATERIALS AND METHOD

The patients included in the study were divided into two groups and were included in the study after signing an informed consent. The study group consisted of 59 subjects, with stage 5D CKD (hemodialysis) and periodontal disease, selected from the patients of the "Fresenius Nephrocare" Dialysis Centers of Parhon Hospital, Iasi. The exclusion criteria were: refusal of participation, absence of all teeth and significant other diseases that prevented examination. Demographic data, health status and biochemical determinations were obtained from the patients' chart and from the electronic database of the dialysis center.

The subjects underwent a general dental and periodontal examination. The missing teeth and the presence of fixed and/or mobile dental prosthetics were noted. Each present tooth was evaluated from a periodontal perspective, through probing with a Columbia probe, determining the following parameters:

a. Periodontal Disease Index, with *gingival and periodontal component, *biofilm component and *calculus component

b. Dental mobility

c. Bleeding on probing (BOP)

d. Inflammatory hyperplasia

e. Gingival recession (measured in mm form the CEJ)

f. Probing depth (PD) (measured in mm, in two sites for single root teeth and in three sites for multiple root teeth).

g. Attachment loss (the sum of gingival recession and the deepest probing site).

A pocket depth - PPD over 2 mm was considered pathological. Considering the deepest probing site and the number of missing teeth, the progression of periodontal disease was classified as mild, moderate and severe.

The control group consisted in 20 patients with periodontal disease, but with no general health issues, chosen among the individuals that came for periodontal treatment to various dental private practices in Iasi. These patients underwent dental and periodontal evaluations similar to those for the study group.

Both groups filled out a questionnaire about their diet, oral hygiene habits and their access to dental services.

RESULTS

In the study group gender distribution was balanced (47.4% females, 52.6% males), and the median age was 58.5. The median dialysis period was 10.8 months. Most of the patients came from a rural background (79.6%) and a similar percentage had cardiac involvement (72.8%). Only 19 patients (32.2%) also had diabetes mellitus.

General dental status

Twenty-two patients exhibited dental treatments in their health history (fillings, root canal treatments) both in the maxilla and the mandible. Eleven patients have had fixed prosthodontics in the maxilla, and 12 patients had similar treatments in the mandible. On the other side, eleven patients had mobile prosthodontics in the maxilla and nine in the mandible.

Over half of those included in the study were partially edentulous in the maxilla (n = 40) and mandible (n = 49). Only thirteen and nine patients, respectively, had no missing teeth.

Periodontal status

All the patients included in the study and control group exhibited signs of PD. In the study group, 75% of the existing teeth had sign of inflammation (bleeding, hyperplasia). Median dental mobility was 1.35. Gum hyperplasia was present in 43% of the teeth; bleeding was present in 61.3%. Median gingival recession was 1.6 mm. Mean probing depth was 2.5 mm, with a mean attachment loss (AL) of 3.7 mm. The most frequent missing tooth was the first upper molar (35%), followed by the first lower molar (31%). The detailed results for each case are exhibited in Table 1

Case	Mobility–score (mean value)	Gingival hyperplasia (yes/no)	Bleeding (yes/no)	Gingival recession – mm (mean)	PPD–mm (mean value)	AL - mm (mean value)
1	1.74136	-	+	1.091474	2.023711	3.588861
2	1.768242	+	+	2.694227	0.34683	4.867094
3	1.072481	-	+	1.915768	4.318854	1.666314
4	2.458189	-	+	2.671802	4.236209	5.492733
5	1.765416	+	+	1.855774	3.782087	4.593711
6	0.367735	+	+	1.394351	0.9601	0.769721
7	0.383733	+	-	2.379506	2.749919	6.888142
8	0.533754	+	-	2.349332	2.921379	3.100329
9	1.372837	-	+	2.598766	0.353494	6.803588
10	1.012364	-	+	1.351233	3.924939	1.060314
11	0.490813	-	+	0.951964	3.663232	1.856058
12	2.026557	+	+	2.191828	1.895424	4.870764
13	1.59867	+	+	0.690871	1.402211	3.569478
14	1.985982	+	+	0.540579	1.342362	5.001995
15	1.702657	-	+	1.097312	0.919019	0.929397
16	1.360395	-	+	1.881244	4.018061	5.253264
17	0.621825	-	+	1.929419	0.755306	6.397272
18	2.248056	+	+	1.521918	1.877618	0.824045
19	1.395028	+	-	1.300782	3.875468	4.65014
20	0.428187	+	+	0.080071	4.013484	3.427974
21	1.216324	+	+	2.176385	3.233286	6.320597
22	1.813313	-	+	0.445614	3.032709	4.760362
23	0.614867	+	+	2.748921	2.063753	1.401171
24	0.546098	+	+	1.318823	2.269891	0.65009
25	2.63779	-	+	2.111588	3.012349	1.515714
26	1.513895	-	-	2.394358	2.371233	0.203595
27	1.151332	-	+	0.671269	1.051959	1.351981
28	0.984754	+	+	2.735221	4.49827	1.438623
29	1.347764	+	+	0.365819	1.975177	5.094589

30	1.14421	-	+	1.450864	4.514549	3.051162
31	1.784677	-	+	2.707335	3.153544	0.926149
32	2.583154	+	+	2.449927	1.978605	4.640175
33	1.982218	+	+	0.100326	2.691839	3.070806
34	0.441576	+	+	0.634088	4.912214	6.949586
35	2.218073	+	+	1.177381	2.019745	7.100602
36	2.404367	+	-	2.399529	0.721539	5.678661
37	2.226566	+	+	1.759041	3.593787	7.054431
38	0.599335	-	+	0.229231	1.013276	0.629125
39	2.277749	-	+	1.747968	3.47235	4.138452
40	0.560558	+	+	1.534806	3.82372	1.319995
41	2.508464	+	-	2.256066	0.602296	5.983795
42	2.166442	-	-	1.328136	4.035654	5.97072
43	0.224023	-	-	2.812148	2.085476	2.91757
44	2.255855	-	+	1.502707	1.567804	4.873731
45	1.51745	-	-	0.980987	1.211992	0.053675
46	0.19839	-	+	2.355938	0.543062	2.396146
47	1.563516	+	+	1.361734	2.11275	1.466604
48	0.502838	-	+	0.179355	4.661516	6.761548
49	0.503606	+	+	0.703752	0.358897	2.807698
50	2.42706	+	+	2.340617	0.648879	4.189763
51	0.220188	-	+	2.332862	3.60591	6.407914
52	0.26908	-	+	2.37697	4.456363	6.911915
53	0.21795	-	-	1.927109	0.781247	3.436364
54	1.111371	+	+	1.966005	2.681718	3.049745
55	2.193438	+	+	1.947522	4.565937	2.318836
56	1.162263	-	+	1.320847	2.649377	4.651917
57	1.486741	+	+	0.855411	2.844965	1.897795
58	1.459423	-	+	1.684035	2.346335	6.160502
59	1.279005	+	+	0.521082	0.95632	3.136704

*+ = yes, - = no

Periodontal involvement was classified into 3 categories, according to disease extent (number of missing/affected teeth) and its severity (PPD, BOP, mobility, recession): mild, moderate and severe (Table 2). In the study group, 4 patients had a mild form of periodontitis (6.77%), 22 a moderate form (37.28%) and 33 a severe form (55.93%) (Fig. 1).

Fig. 1. Distribution of periodontal disease stages in the study group.

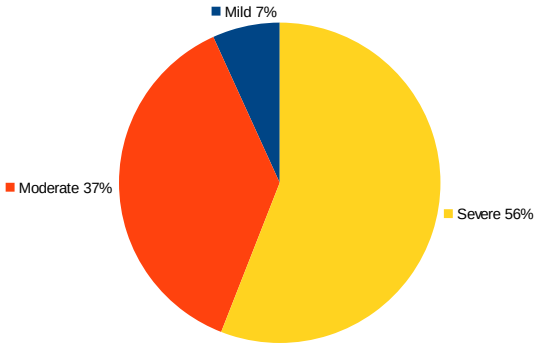

Table 2. Diagnosis characteristics for evaluating the severity of PD (AAP Task Force Report, 2015).

	Mild	***Moderate***	***Severe***
Probing depth	3-5 mm	5-7 mm	Over 7 mm
Bleeding on probing	Yes	Yes	Yes
Radiographic bone loss	Up to 15% of root length or 2-3 mm	16-30% or 3-5 mm	Over 30% or over 5 mm
Clinical attachment loss	1-2 mm	3-4 mm	Over 5 mm

As for the control group, the median age was 41.75 years, the individuals coming mainly from the urban environment (92.1%). Out of 20 patients, only 10% had dental treatments; 20% had fixed maxillary and mandibular prosthodontics and only 1 case had mobile prosthodontics in both, maxilla and mandible. Only 5 cases had no missing teeth, the rest displaying partial tooth loss.

Over 80% of the present teeth in the control group had signs of inflammation. Mean dental mobility was 1,2. Gingival hyperplasia was present in only 30% of the teeth. Gingival bleeding was identified in only 74.5% of the present teeth. Median gingival recession was 1.3 mm, with a median pocket depth (PPD of 3.1 mm and an attachment loss of 3.5 mm. The most frequent absent tooth was the first upper molar (23%). Detailed results for each case are presented in Table 3.

Table 3. Control group periodontal status

Case	**Mobility–score (mean)**	**Gingival hyperplasia (yes/no)**	**Bleeding (yes/no)**	**Gingival recession – mm (mean)**	**PPD–mm (mean)**	**AL - mm (mean value)**
1	0.301033	-	+	0.485699	0.87526	1.520761
2	0.541867	+	+	0.491875	0.990799	2.31533
3	0.556388	-	+	0.255034	1.333752	1.095445
4	0.382186	-	+	0.109191	0.926112	1.3424
5	0.83945	+	+	0.677694	1.288686	0.943394
6	0.344429	+	+	0.792307	0.265756	0.601536
7	0.756966	+	-	0.896711	1.325715	0.612664
8	0.774332	+	-	0.66537	0.325972	1.917438
9	0.829592	-	+	0.007072	1.296175	1.546751
10	0.859329	-	+	0.067036	1.787269	1.614866
11	0.542724	-	+	0.865176	1.333837	0.634508
12	0.140647	+	+	0.193832	0.843395	1.661009
13	0.326011	-	+	0.553394	0.469082	2.190804
14	0.400376	-	+	0.348641	0.411669	1.355583
15	0.353343	-	+	0.276246	1.261792	2.158426
16	0.56879	-	+	0.738501	0.998765	0.373228
17	0.356841	-	+	0.658201	1.331785	1.230283
18	0.056652	-	-	0.829901	0.128182	0.819343
19	0.346393	-	-	0.343278	1.928873	1.039998
20	0.783388	-	-	0.913513	1.434896	0.347948

According to the three categories of PD classification, most of the cases (76%) presented a moderate form of periodontitis, 14% had a mild form and only 10% displayed severe form (Fig. 2).

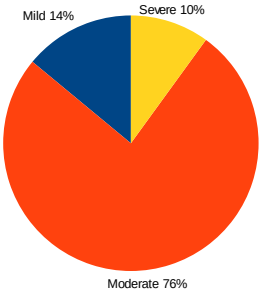

Fig. 2. Distribution of periodontal disease stages in the control group

DISCUSSION

The existing studies are extremely contradictory when considering the relationship between CKD and periodontal disease. The association between periodontitis and CKD is based on the idea that different types of acute and chronic inflammation may stimulate an inflammatory response in the kidneys, with the potential of kidney failure development. The prevalence of periodontal involvement in CKD patients may be due also to the association with malnutrition and low socio-economic status, as well as low access to dental services and oral hygiene.

A metanalysis published in 2014 reviewed eighty-eight studies in 125 population groups (1134 adults), most of the studies concentrating on end stage CKD adults (90 population groups), with a lower number of oral health evaluations in those with CKD stage 1 to 5 (only 14 populations) (Ruospo et al., 2014). Studies were, in general, smaller, and the duration of dialysis was between 0 and 125 months. Periodontal disease affected 31,6% of 1 to 5 stage CKD (5 populations) (Fisher et al., 2008; Ioannidou et al., 2011; Vesterinen et al., 2011) and 56,8% in 5D CKD (Bouattar et al., 2011; Castillo et al., 2007; Chen et al., 2006; Cunha et al., 2007; Dag et al., 2010; de la Rosa et al., 2008; Franek et al., 2006; Goncalves et al., 2011; Siribamrungwong & Puangpanngam, 2012).

Periodontal disease prevalence in end stage CKD was not influenced by age, but grew proportionate with female gender and dialysis duration. Periodontal probing depth (PPD) was, as well, a measure of periodontal health as it described the depth of the gingival sulcus along which the bacterial biofilm can migrate along the root surface. In CKD populations, mean PPD was 2.3 mm (26 population groups) in end stage CKD (Bayraktar et al., 2009; Chamani et al., 2009; Dag et al., 2010; Sekiguchi et al., 2012) and 0.7 and, respectively, 2.4 mm in CKD populations stage 1 to 5 (Garcez et al., 2009).

Clinical attachment loss (CAL) is the extend of periodontal structure loss around the teeth. In the limited data in dialysis patients, mean CAL was 3.5 mm in ten populations (Chamani et al., 2009).

An issue with CKD in the context of global kidney-cardiac-vascular disease is represented by cardiovascular and all-cause mortality. Ruospo identifies two studies

which described this risk and indicate as well a constant risk of all-cause and cardiovascular mortality in moderate to severe periodontal disease, compared to healthy or mild periodontitis patients (Ruospo et al., 2014).

Another metanalysis identifies 2456 eligible articles about the CKD-PD interaction, out of which 4 were cross-sectional, one retrospective and 3 interventional. This metanalysis identifies a bidirectional relationship between the two clinical entities and positive results of PD treatment on CKD (Chambrone et al., 2013). Most observational studies agree that the individuals with periodontal disease have a higher risk of CKD (Fisher et al., 2008, Grubbs et al., 2012).

Low oral hygiene, as evidenced by the high frequency of missing teeth, is a constant in CKD patients. The DMF index (decayed, missing, filled teeth) comprises dental health status, as used in multiple studies. Grubbs, for example, indicates the fact that the number of absent teeth is higher and that of treated teeth is lower than that in the general population of the U.S., which can indicate a lower access/use of dental health services (Grubbs et al., 2012).

A series of predisposing and progression accelerating factors for the periodontal disease can be found in patients with CKD, including low immunity and healing, diabetes mellitus, smoking, low dental hygiene, xerostomia and malnutrition (National Kidney Foundation, 2002, Albandar, 2005). The literature review proves that there are high variations between the estimates of oral diseases, directly linked to the area from which the patient comes from, age, dialysis duration.

It is considered that PD can offer support elements for nephropathy and end stage CKD development (Shultis et al., 2007). In the case of diabetes, as an additional risk factor, hyperglycemia has an important role in CKD development (The Diabetes Control and Complications Trial Research Group, 1993) and is associated with PD (Taylor, 2006). Periodontal extraction therapy and other mechanic procedures and local antibiotics determine the reduction of inflammatory biomarkers (Taylor et al., 2006).

The dental profile of the CKD patient involves multiple dental extractions – between 20 and 40 percent (Fisher et al., 2008). The DMF index was directly proportional with age, but was not associated with gender or dialysis duration. Our study only used the M (missing teeth) component to evaluate the patients' dental status.

Oral health evaluation is extremely rare for those with CKD, especially in end-stages. The affirmation that an altered oral status is frequent in CKD adult is relevant for new priorities in research in the field of kidney disease. Impaired oral health status and severe PD, are associated with other negative prognosis factors for CKD patients, such as malnutrition and inflammation. Thus, it is justified to consider that a low oral health may determine events that lead to kidney disease, through modifications that determine endothelial dysfunction, atherosclerosis (Lalla et al., 2003), endotoxins and chronic inflammation (Beck et al., 2005).

Although there is numerous information about oral diseases as a determining factor for general health, data about the correlation between oral health and CKD mortality are based on a small number of studies, limited to PD. Further data is needed, which should include larger CKD populations, to better understand the association between oral status and clinical results in this population category. This may justify further research about treating dental

and PD in CKD context.

Global determining factors for oral health are complex and include and oral health factors, including real and perceived barriers for care and political and environment issues, such as nutrition and fluoridation (Petersen, 2005). International experience suggests that social and economic gradients significantly influence adult oral health, even in the presence of public oral health programs in childhood, which is also relevant for CKD patients.

In all countries and health systems, a better control of dental status from the social and economic factors point of view of, is found in adults that have a prophylactic attitude towards dental care and who use regularly other means of dental hygiene than just brushing. This data, together with the studies in this review, suggest that the risk factors for oral diseases in coexisting CKD may be complex and that health policies should adapt to these conditions.

Our results are mostly consistent to those from the literature data, at least for the study group. All those include in this group had both end stage CKD and PD. Other risk factors for both disease, cardiovascular involvement and diabetes mellitus, were present in significant percentages. This may support the hypothesis of a bidirectional relationship between CKD and other chronic inflammatory entities with cumulative and kidney disease potential.

Considering the direct relationship between female gender and periodontitis, our data did not show a direct correlation, but the group's gender distribution was balanced, which may indicate that this type of data is dependent on study design.

In our study, the analysis from a social and economic perspective of the CKD and periodontal disease patient indicated a prevalence in the male gender (but minnor difference) from a rural background, most likely due to low access to oral hygiene products and to dental care services, or to low economic status. This fact is observed in the dental status, where more than half of the study group had missing teeth.

Because of the limits of the examining conditions – during hemodialysis – we were only able to evaluate exclusively the missing teeth (M) component of the DMF index. On the other hand, we registered globally the presence or absence of dental treatments in the maxilla and mandible, their percentages being low and thus suggesting a difficult access to dental care, due to low income, low education or limits imposed by the clinical status of hemodialysis. Periodontal health evaluation offered similar results to those in earlier studies, regarding tooth mobility, bleeding on probing, hyperplasia, probing depth and CAL.

For the control group, most of the patients were female, from an urban background. We can thus identify an opposition between the profile of the patient in each group. Although median age was lower for the control group, dental status was similar to that in the study batch.

Over half of the patients had some missing teeth, but the prevalence of dental treatments was lower. This may be explained by the lower median age of the group and better access to dental care. It is possible that the better general health status and the higher social and economic status may contribute to this data. Periodontal status data are similar to the study group, with values close to those found in the literature.

Thus, we may assume that the existing differences between the two groups may be due first of all to associated and general status factors, but also to the social and economic status of the patients. There is still the need for further evaluation of the existing data and of possible correlations

between recorded values. Also, it would be of further reference to link clinical data to GCF inflammatory biomarkers and to subjective patient data

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