

## THE SIGNIFICANCE OF DENTAL FOCI IN GLOMERULAR NEPHROPATHIES

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**Summary.** *In our study we want to reveal the role of dental foci, compared to other localized infections, in the evolution of glomerular nephropathies. Therefore we followed up the link between the presence of these foci and the flare-up of glomerular nephropathies, with or without renal failure.*

*A number of 328 patients with glomerulonephritis, primary or secondary, hospitalized in the Nephrology Department of Timisoara during the period 1997-2002, were studied retrospectively. The patients were split up in 4 groups.*

*The 240 patients of the control group (glomerulonephritis without any infection) had the following mean values of BUN, serum creatinine and proteinuria:  $84.10 \pm 69.85$  mg%,  $3.11 \pm 2.97$  mg%,  $2.33 \pm 1.79$  g/24h.*

*In the 52 patients with infections other than dental foci we observed, after antibiotic treatment, a statistically significant decrease of proteinuria (from  $2.51 \pm 1.75$  g/24h to  $1.96 \pm 1.27$  g/24h) and of BUN (from  $125.10 \pm 78.97$  to  $104.3 \pm 63.25$  mg%).*

*In the 16 patients with dental foci associated with other infections we observed, after antibiotic  $\pm$  stomatologic treatment, a statistically significant decrease of proteinuria ( $2.34 \pm 1.74$  g/24h-  $1.76 \pm 1.4$  g/24h).*

*Concerning the 20 patients with dental foci, mean proteinuria decreased from  $2.11 \pm 1.63$  g/24h to  $1.79 \pm 1.26$  g/24h.*

*In some patients, after stomatological treatment, we observed an increase of proteinuria, BUN or serum creatinine, possibly due to the treatment of the localized infection, despite a correct prophylactic antibiotic treatment that could not prevent interactions of the dental foci with the kidney.*

**Key words:** *Glomerulonephritis, dental foci, localized infections, antibiotic prophylaxis*

### Introduction

In the pathogenesis and evolution of glomerular nephropathies, localized infections play an important role. Attention is usually focused on upper respiratory tract infections (pharyngeal, tonsillar and sinus), less importance being given to dental foci. Because in the clinical practice the latter are frequently found associated with glomerulopathies, we tried to analyze their incidence, and at the same time the evolution of the renal disease after a specific stomatologic treatment of dental foci.

Renal patients appear to be predisposed to a variety of dental problems such as periodontal disease, narrowing of the pulp chamber, enamel abnormalities, premature tooth loss and xerostomia (1).

A normal healthy person is colonized by aerobic and anaerobic bacteria in the mouth. These bacteria, and particularly *Streptococcus mutans*, contribute to a dense microbial mass called dental plaque, a major cause of tooth decay (2).

Infections in the mouth can develop into chronic localized infections. The dental surface represents a good environment for bacterial colonization, and for the formation of dental plaque.

It is a known fact that there is a close link between dental plaque formation and periodontopathies. The latter develop as a result of complex interactions be-

tween the host and the local dental plaque. The infections can localize in the pulp of a tooth, developing acute pulpitis. On the other hand, a chronic evolution could lead to the formation of dental granuloma; in this case the infection could last longer. In the evolution of these infections acute phases may occur, despite the fact that the organism tries to isolate these foci by forming an external layer of fibrin and connective tissue. In these phases, germs or parts of them- toxins, that is, could get into the circulation. They could produce various lesions in other tissues, either directly or indirectly, by forming immune complexes. These are deposited in different tissues, where they can activate different factors, like the complement. The kidneys could represent the target organ in this process.

This mechanism is described during the course of upper respiratory tract infections: tonsillitis, pharyngitis, sinusitis, otitis as well as visceral infections, which could develop into abscesses, like suppurated appendicitis, for example.

Chronic foci are frequent, and they are defined as localized chronic inflammatory processes, which through different pathogenic mechanisms can develop vegetative disorders, vascular disorders, and lesional manifestations.

The diagnosis and correct treatment of infectious foci with a role in the etiology or progression of glomerular

nephropathy is very important. Concerning the relationship of chronic foci with glomerulonephritis, Lagrue et al. showed that many patients with IgA nephropathy have a chronic infection (e.g. dental abscess, chronic sinusitis or cryptic tonsillitis) (3), with about 40% of patients with IgA nephropathy experiencing recurrent macroscopic haematuria, which occurs within 48 hours of an infection. The suggestion has been made that tonsillectomy may remove the bacterial foci and result in decreased proteinuria and stabilization of renal function (4).

The stomatologic treatment itself could intervene in the evolution of the renal disease. Transient, usually asymptomatic bacteremias occur in a wide variety of dental manipulations, particularly those involving the mucous membranes. Therefore, antimicrobial prophylaxis is essential when these patients undergo dental procedures - causing bacteremia (5). ESRD patients, particularly those with an arteriovenous shunt for hemodialysis access, are predisposed to valvular endocarditis. Thus, BE prevention is the primary goal of antibiotic prophylaxis prior to dental or other invasive procedures in these patients (6). The goal of treatment is to restore maximum function while minimizing the risk of oral infection (7).

Not always are localized infections diagnosed at the onset of the disease and they could be found during the evolution. Therefore a patient with glomerulonephritis should be investigated in order to detect the infection which was the cause of its acutization.

Until now there has been insufficient data concerning the role of dental foci in the pathogenesis of glomerular nephropathies.

### Aim of the Study

In our study we want to reveal the role played by dental foci, compared to other localized infections, in the evolution of glomerular nephropathies. Therefore we followed up the link between the presence of these foci and the flare-ups of glomerular nephropathies, with or without renal failure.

### Material and Methods

A number of 328 patients with glomerulonephritis, primary or secondary, hospitalized in the Nephrology Department of Timisoara during the period 1997-2002, were studied retrospectively. From our database we

used the following information concerning each patient: the morphopathological type of the glomerular lesion (in those cases where a kidney biopsy was available), the type of localized infection associated, biological data (proteinuria, BUN, serum creatinine) at admission into the hospital and after the treatment of the various infections.

The patients were split up into four groups (Table 1):

- **Control group:** 240 patients with glomerulonephritis without any infection (106 female + 134 male), with a mean age of  $42.7 \pm 14.45$  years
- **Group A:** 52 patients with infections other than dental foci (26 female+ 27 male) with a mean age of  $40.65 \pm 12.87$  years
- **Group B1:** 16 patients with dental foci associated with other infections (7 female+ 9 male) with a mean age of:  $42.88 \pm 15.29$  years
- **Group B2:** 20 patients with dental foci (9 female+ 11 male) with a mean age of:  $38.5 \pm 13.5$  years

The mean values of the data were compared using the Student t test.

### Results

In 85 patients of the **control group** (240 patients with glomerulonephritis without any infections) echoguided kidney biopsy was performed, with the following results: mesangial proliferation - 25 patients, mesangiocapillary - 33, membranous - 12, minimal change - 2, focal segmental glomerulosclerosis - 9, focal proliferation - 1, endo and extra capillary proliferation - 1, not classifiable lesions - 2 (see Table 2). Of the 240 patients, 160 had renal failure and 56 nephrotic syndrome. Mean values of BUN, serum creatinine and proteinuria in this group were:  $84.1 \pm 69.85$  mg%,  $3.11 \pm 2.97$  mg%,  $2.33 \pm 1.79$  g/24h.

In the patients of **group A** (52 patients with localized infections, other than dental foci) we found upper respiratory tract infections (24 patients), urinary tract infections (11), pulmonary (4), gynecological (2), dermatological (1) and associated infections (10). The patients with primary chronic glomerulonephritis in this group (32-with kidney biopsy) showed the following histopathological forms: mesangial proliferation - 14 patients, mesangiocapillary - 5, membranous - 4, focal segmental glomerulosclerosis - 7, focal proliferation - 1,

Table 1. Groups under study

Groups	CG No infections	A Other infections	B1 Dental foci + other infections	B2 Dental foci
No. of patients	240	52	16	20
Mean age	$42.7 \pm 14.4$	$40.6 \pm 12.8$	$42.8 \pm 15.2$	$38.5 \pm 13.5$
Fem: male ratio	106:134	26:27	7:9	9:11
Mean BUN (mg/dl)	$84.10 \pm 69.85$	$71.39 \pm 67.32$	$60.57 \pm 35.59$	$86.9 \pm 36.9$
Mean serum creatinine (mg/dl)	$3.11 \pm 2.97$	$2.23 \pm 2.21$	$1.63 \pm 0.94$	$2.88 \pm 1.77$
Mean proteinuria (g/24h)	$2.23 \pm 1.79$	$2.51 \pm 1.75$	$1.76 \pm 1.40$	$2.11 \pm 1.63$
patients with CRF	160	21	8	10
patients with nephrotic syndrom	56	9	4	5

not classifiable lesions - 1. The other patients presented with acute GN-1, SLE-2, diabetic nephropathy - 1, vasculitis - 2, amiloidosis - 1 and in 11 patients no secondary cause of GN was found and no biopsy was performed (see Table 2). Of the 52 patients, 21 showed renal failure and 9 nephrotic syndrome.

Table 2. Kidney biopsy diagnoses in each of the four groups (CG- control group, A- group with other infections, B1- group with associations of dental foci and other infections, B2- group with dental foci)

	CG	A	B1	B2
mesangial proliferation	25	14	4	6
mesangio-capillary	33	5	1	4
membranous	12	4	2	0
minimal change	2	0	0	3
focal segmental glomerulosclerosis	9	7	0	0
not classified	2	1	0	0
focal proliferation	1	1	0	0
endo- and extracapillary proliferation	1	0	0	0
primary GNs - total	85	32	7	13
acute GN		3	0	0
SLE		2	2	1
diabetic nephropathy		1	0	0
vasculitides		2	1	0
amiloidosis		1	0	0
No kidney biopsy	155	11	6	6
TOTAL	240	52	16	20

Proteinuria was followed up in 36 out of 52 patients (69.2%) after the antibiotic treatment of the infections. The mean value of proteinuria decreased statistically significantly in these patients:  $2.51 \pm 1.75$  g/24h to  $1.96 \pm 1.27$  g/24h ( $P < 0.05$ ) (see Figure 1). In 8 of the patients (22.22%) proteinuria increased, in 10 patients (27.77%) it remained constant, while in 18 patients (50%) we observed a decrease of proteinuria.

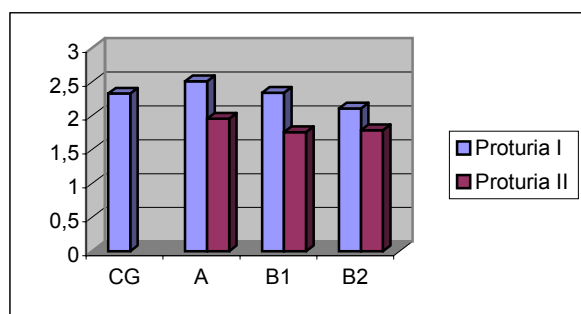


Fig. 1. Comparison of mean proteinuria in the control group (CG), with the values before (Proturia I) and after treatment of the infectious foci (Proturia II), in the three studied groups (A, B1, B2).  $P < 0.05$  for groups A and B1.

Concerning the 21 patients with renal failure, the mean values of BUN and serum creatinine decreased: BUN ( $125.1 \pm 78.97$  to  $104.3 \pm 63.25$  mg%) (see figure 2), serum creatinine ( $4.1 \pm 2.4$  to  $3.8 \pm 3$  mg%) (see figure 3); but the difference was statistically significant only in the case of BUN ( $P < 0.05$ ). We found an increase of the

values in 5 patients (23.80%), a decrease in 11 patients (52.38%), and no change in 5 patients (23.80%).

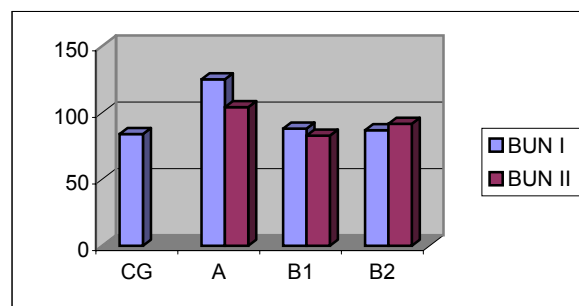


Fig. 2. Comparison of mean BUN in the control group (CG), with the values before (BUN I) and after treatment of the infectious foci (BUN II), in the three studied groups (A, B1, B2).  $P < 0.05$  for group A.

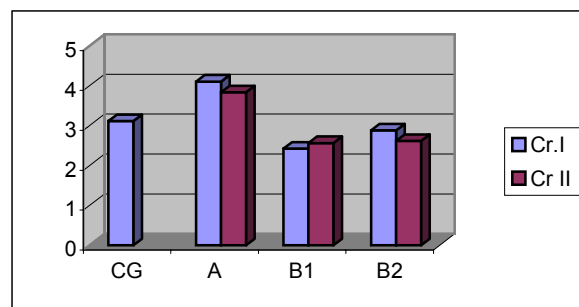


Fig. 3. Comparison of mean serum creatinine in the control group (CG), with the values before (Cr.I) and after treatment of the infectious foci (Cr.II), in the three studied groups (A, B1, B2). There are no statistically significant differences.

As stated before, the patients with dental foci (36 patients) were split up in 2 groups: group B1- the patients with dental foci associated with other localized infections; and group B2- the patients who presented dental foci without other infections.

The 16 patients of the **B1 group** showed alongside dental foci the following localized infections: upper respiratory tract infections (7), urinary tract infections (7), pulmonary infections (1), and an association of upper respiratory tract and urinary tract infection. All patients underwent antibiotic treatment, while in 6 of them specific stomatologic treatment was required.

The patients with primary chronic glomerulonephritis in this group (7-with kidney biopsy) showed the following histopathological forms: mesangial proliferation - 4 patients, mesangiocapillary - 1, membranous - 2. The other patients showed SLE - 2, Wegener disease- 1 and in 6 patients no secondary cause of GN was found and no biopsy was performed (see Table 2). In this group 8 patients showed renal failure and 4 nephrotic syndrome.

In 13/16 patients the evolution of proteinuria before and after treatment was followed up, and a statistically significant decrease of the mean values resulted:  $2.34 \pm 1.74$  g/24h -  $1.76 \pm 1.4$  g/24h ( $P < 0.05$ ) (Fig. 1). In 2

patients (15.4%) proteinuria increased, in other 2 patients remained constant (15.4%), while in 8 patients (61.5%) there was a decrease of proteinuria. In one patient (7.7%), however, proteinuria decreased only after an initial increase.

In the 8 patients with renal failure we had the following changes of the mean values of BUN and serum creatinine: BUN ( $88.16 \pm 27.94 - 82.85 \pm 44.99$  mg%) (Fig. 2), serum creatinine ( $2.42 \pm 0.66 - 2.56 \pm 0.96$  mg%) (Fig. 3). None of these changes are statistically significant using the Student's t test. Taken individually, we had an increase in 2 patients (25%), a decrease in 4 patients (50%) and no change in another 2 patients (25%).

All the patients of the **B2 group** (with dental foci without other localized infections) underwent antibiotic treatment, in 10 of them a stomatological approach had to be added. The patients with primary chronic glomerulonephritis in this group (13 - with kidney biopsy) showed the following histopathological forms: mesangial proliferation - 6 patients, mesangiocapillary - 4, minimal change - 3. The other patients showed SLE-1 and in 6 patients no secondary cause of GN was found and no biopsy was performed (Table 2). 10 of the patients in this group showed renal failure, and 5 a nephrotic syndrome.

In 18 out of 20 patients proteinuria was followed up prior and after specific treatment of the dental foci. The mean values decreased from  $2.11 \pm 1.63$  g/24h to  $1.79 \pm 1.26$  g/24h (see Fig. 1); in 5 patients (27.8%) there was an increase, in other 5 patients (27.8%) proteinuria remained constant, while in 6 patients (33.3%) there was a decrease; two patients (11.1%) presented a decrease after an initial increase.

In the 10 patients with renal failure the mean values of BUN and serum creatinine had the following evolution: BUN- ( $86.9 \pm 36.97 - 91.64 \pm 32.03$  mg%) (see Fig. 2), serum creatinine ( $2.88 \pm 1.77 - 2.61 \pm 1.12$  mg%) (see Fig. 3); with an increase in 2 patients (20%), a decrease in 4 patients (40%) and no change in 4 patients (40%).

## Discussion

In our study we diagnosed the presence of dental foci in 36 out of 328 patients with glomerular nephropathies (10.97%). In 20 patients we found dental foci exclusively, while in 16 patients other localized infections occurred.

The importance of dental foci was suggested by the impact on the evolution of renal disease after antibiotic and/or stomatologic treatment: apical resection, drainage of acute abscesses, dental extractions.

In the group with dental foci exclusively, we observed an increase of proteinuria in 27.8% of the patients, which points out the fact that an intervention at the level of the localized infection, despite a correct prophylactic antibiotic treatment, could not prevent interactions of the dental foci with the kidney.

On the other hand, in 6 patients (33%) we had a decrease of proteinuria after specific treatment (antibiotic

and/or stomatologic) which could point out the role played by dental foci in the glomerular pathology.

The consequence of the treatment of a localized infection could be an initial increase followed by a decrease of proteinuria, which leads us to conclude that a complex approach to these foci (stomatological associated with antibiotic treatment) could be necessary.

In some patients the specific treatment did not have any influence on proteinuria. This could be due to the fact that either dental foci have no relation with the glomerular disease, or these foci are not active at the moment of therapeutic approach.

Besides proteinuria, dental foci seem to have great importance in the renal function of CRF patients, as in 4 out of 10 patients we found a decrease of BUN and serum creatinine after the treatment of dental foci. This could be a result of the positive effect of treatment, because no other factors intervened in the course of CRF. In another 4 patients we didn't observe any changes, while in 2 patients we found an increase of BUN and serum creatinine. The alteration of renal function could be explained by the possible mobilization of germs from dental foci, which could lead to an active state of the disease.

A good example, which emphasizes the previous statement could be the case of a patient recently admitted to our department with chronic glomerulonephritis, CRF with a recently discovered proteinuria of 2 g/24h. In our search for a localized infection, we found dental foci. After the stomatological treatment the patient developed fever -  $39^{\circ}$  C, for 3 days, and an increase in serum creatinine from 7.76 mg% to 9.3 mg%. Under the initial antibiotic treatment (cephalosporins - Maxil) fever did not decrease, this happened only after the association of quinolones (ciprofloxacin). The latter is known for its capacity to penetrate tissues, including bone and dental.

In the second group of patients with dental foci associated with other localized infections, a number of 8 out of 16 showed upper respiratory tract infections, known for their potential role in the pathogenesis of glomerulonephritis.

In these patients (16) we encountered a similar evolution with that of the previous group, who had only dental foci. In 2 out of 13 patients (15.4%) proteinuria increased, in other 2 patients it remained constant (15.4%), while in 8 patients (61.5%) there was a decrease of proteinuria. In one patient (7.7%), however, proteinuria decreased only after an initial increase.

It is worth mentioning that the treatment of upper respiratory tract infections was with antibiotics.

It could not be demonstrated that the association of two localized infections increased the risk of glomerular injury. In some patients, who were treated by stomatological means and in whom the infection was active, we observed a positive effect, while in others flare-up of the glomerular disease occurred (3 cases, but 1 recovered after antibiotic treatment).

We observed similar changes concerning the renal function. We had an increase of BUN and serum creatinine in 2 patients (25%), a decrease in 4 patients (50%) and no change in another 2 patients (25%).

Other localized infections, besides upper respiratory tract infections, were found in the studied patients: urinary tract infections in 8 out of 16 patients, pulmonary infections in 1 patient. These infections could have also intervened in the evolution of glomerular nephropathies through various mechanisms.

The group of 52 patients with localized infections, other than dental foci, was dominated by upper respiratory tract infections - 24 patients, urinary tract infections - 11 patients, pulmonary infections - 4 patients, gynecological infections - 2 patients, dermatological infections - 1 patient, associated infections - 10 patients.

The evolution of proteinuria, BUN, serum creatinine among them was similar to that in the groups of patients with dental foci.

In most patients with glomerulonephritis, we did not find any localized infections: 240 patients (73.17%),

despite systematic investigations performed in our department. This could be due to the fact that infections are absent or that they occurred in a different period than the one in which we explored the patients.

## Conclusion

The purpose of this study is to point out the importance of finding and treating dental foci correctly. It is difficult to define these cases, as well as the localized infection we described above, but these infections could not be ignored.

At least in some patients, dental foci play an important role in the evolution of glomerular nephropathies. These foci should be recognized and treated carefully under antibiotic protection, in a stable stage of the disease. The persistence, aggravation and recurrence of dental foci should lead to a common approach of the nephrologist and the stomatologist, expressing the necessity of a multidisciplinary approach in nephrology.

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## ZNAČAJ DENTALNE FOKALOZE KOD GLOMERULARNIH NEFROPATIJA

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**Kratak sadržaj:** U ovoj studiji mi želimo da ukažemo na značaj dentalnih fokusa, u poređenju sa drugim lokalizovanim infekcijama, u evoluciji glomerularnih nefropatija. Zbog toga smo analizirali povezanost prisustva ovih fokusa i glomerularnih nefropatija, sa i bez bubrežne insuficijencije.

Retrospektivno je analizirano 328 bolesnika sa primarnim ili sekundarnim glomerulonefritom, hospitalizovanih u Odeljenju za nefrologiju u Temišvaru u periodu 1997-2002. Bolesnici su podeljeni u četiri grupe.

Kontrolnu grupu je činilo 240 bolesnika (glomerulonefritis bez infekcije) sa srednjim vrednostima BUN, serumskim kreatininom i proteinurijom:  $84,10 \pm 69,85$  mg%,  $3,11 \pm 2,97$  mg%,  $2,33 \pm 1,79$  g/24h

Pokazano je da kod 52 bolesnika sa infekcijama i bez dentalne fokaloze, posle lečenja antibioticima statistički značajno se smanjuje proteinurija (od  $2,51 \pm 1,75$  g/24h na  $1,96 \pm 1,27$  g/24h i BUN (od  $125,10 \pm 78,97$  na  $104,3 \pm 63,25$  mg%).

Kod 16 bolesnika sa dentalnom fokalozaom udruženom sa drugim infekcijama zapazili smo da posle stomatološkog i tretmana antibioticima dolazi da statistički značajnog smanjenja proteinurije ( $2,34 \pm 1,74$  g/24h –  $1,76 \pm 1,4$  g/24h)

Kod 20 bolesnika sa dentalnom fokalozaom srednja vrednost proteinurije se smanjila sa  $2,11 \pm 1,63$  g/24h na  $1,79 \pm 1,26$  g/24h. Kod nekih bolesnika posle stomatološkog tretmana zabeležen je porast proteinurije, BUN-a ili serumskog kreatinina, verovatno zbog tretmana lokalne infekcije, uprkos adekvatne profilaktičke primene antibiotika koja nije mogla da prevenira interakciju dentalnih fokusa sa bubrežima.

**Cljučne reči:** Glomerulonefritis, dentalna fokaloza, lokalizovana infekcija, antibiotska profilaksa