

## ENDOSCOPIC FINDINGS IN THE PROXIMAL PART OF THE DIGESTIVE TRACT IN PATIENTS WITH CHRONIC RENAL FAILURE UNDERGOING CHRONIC DIALYSIS PROGRAM

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**Summary.** *A prospective study included 30 patients with chronic renal insufficiency undergoing chronic chemodialysis, with or without digestive problems, who underwent proximal endoscopy for pretransplantation balance in the period 1998-2000. The study included patients admitted to the Institute of Nephrology and Chemodialysis of the Clinical Centre in Nis and Nephrology Clinic of the Clinical Centre of Serbia, Belgrade. The control group was composed of 21 patients with no chronic renal insufficiency treated and examined at Gastroenterology and Hepatology Clinic of the Clinical Centre in Nis who underwent proximal endoscopy. The patients were randomly selected. By proximal endoscopy performed in patients undergoing chronic dialysis, the following pathological changes were confirmed: erosions in 9 (30%), angiodysplasias in 2 (6.67%), ventricular ulcers in 1 (3.33%), duodenal ulcers in 1 (3.33%), ventricular polyps in 1 (3.33%), and a regular finding was established in 16 (53.34%) patients. External factors contribute to gastrointestinal changes: moderate quantities of alcohol consumption, smoking cigarettes, various drugs intake, and non-observance of dietetic regime. These risk factors also contribute to deciding on the performance of proximal endoscopy. The presence of the subjective problems with the digestive tract, along with the objective finding in the patients on chemodialysis are indications for proximal endoscopy aimed at prevention, and early detection of changes in the digestive tract. According to our investigation, the indications for proximal endoscopy in patients undergoing chronic hemodialysis are: patients on dialysis for 0-2 years, frequent digestive problems but not closely associated with uremic toxicity, acute gastrointestinal symptomatology (stomach aches, hematemesis, melena...etc), pretransplantation balance and patients with chronic systemic disease that receive immunosuppressive therapy for 6 months.*

**Key words:** *Endoscopic changes, chemodialysis, proximal endoscopy*

### Introduction

The performance of flexible endoscopy has brought significant changes in gastroenterology. Endoscopic examinations put patients at no risk of irradiation, but sensitivity and specificity are much higher in comparison to x-ray examination of the digestive tract, particularly in smaller lesions. In the case of digestive bleeding, there is a high probability of detecting bleeding lesions. In addition, therapeutic endoscopy now available, is of high importance in conditions such as bleeding lesions, polyps, etc., which, until recently, demanded surgery (1).

Chemodialysis represents a kind of active treatment of terminal phase HBI. It is a process of diffusion through a semipermeable membrane, removing the unwanted substances from blood, and adding the needed components to blood (1).

In patients with HBI, the occurrences of digestive problems such as nausea, loss of appetite and weight, and even digestive tract bleeding are very frequent.

Previous investigations have pointed out an increased incidence of peptide ulcers in patients undergoing dialysis (1), while some of them pointed out to an increased incidence of stomach ulcers as well. Recent investigations have not established an increased incidence of peptide ulcers in patients undergoing dialysis (1).

Several different studies pointed out the occurrence of erosive changes in as many as 50% of patients undergoing dialysis (2). According to one study, even 89% of patients undergoing dialysis had erosive changes in comparison with 21% in the control group (2).

### Materials and Methods

The investigation was carried out on patients admitted to the Institute of Nephrology and Hemodialysis of the Clinical Center Nis and Nephrology Clinic of the Clinical Center of Serbia, Belgrade in the period from 1998-2000. A prospective study included 30 patients

with chronic renal failure undergoing chemodialysis with or without digestive problems that underwent proximal endoscopy for pretransplantation balance.

The control group (group 2) was composed of 21 patients without chronic renal failure, treated and investigated at the Clinic for Gastroenterology and Hepatology of the Clinical Center Nis who underwent proximal endoscopy. Patients were randomly selected.

**Clinical processing**

- Anamnesis
- Physical examination

**Laboratory analysis**

- Erythrocyte sedimentation
- Blood picture
- Biochemical analysis (urea, creatinine bilirubin, transaminases, alkali phosphatases, amylases, cholesterol, triglycerides, glycemia, and electrolytes)
- HBsAg and anti HCV antibodies (in patients undergoing dialysis)
- HLA typization (within pretransplantation balance)

**Proximal endoscopy**

The examination is indicated for the purpose of confirming the clinical diagnosis both in patients with digestive problems and without problems preparing for kidney transplantation. Proximal endoscopy was performed with Olympus endoscope GITQ-30.

**Statistical tests**

The results were computer processed, and the statistically significant differences were determined by means of student's T-test.

**Results**

Personal data of the investigated patients are shown in Tables 1 and 2. A statistically significant difference in the age was found between the patients in group 1 and group 2 ( $p < 0.001$ ).

Table 1. Personal data of the investigated patients

Patients	Group 1		Group 2	
Number	30		21	
Age	39.9±11.6		61.2±13.5	
Sex	Females	8 26.67%	8 38.10%	
	Males	22 73.33%	13 61.90%	

There were 73% of males vs. 27% of females.

In the group, 2.62% were males and 38% females.

Women over 50 years of age were present more frequently (50%), while man aged between 41-50 years (36.82%) were present more frequently.

Table 2. The group 1 patients according to age and sex

Age (in years)	Sex				Total	
	Females		Males		N <sup>o</sup>	%
	N <sup>o</sup>	%	N <sup>o</sup>	%		
Under 20	-		4	18.2	4	13.3
21-30	1	12.5	1	4.5	2	6.7
31-40	1	12.5	7	31.8	8	26.7
41-50	2	25.0	8	36.4	10	33.3
Over 50	4	50.0	2	9.1	6	20.0
Total	8	100.0	22	100.0	30	100.0

Female sex was present only in the age group over 50 years, whereas males were equally present in the age groups 41-50 years and over 50 years, as shown in Table 3.

Table 3. The group 2 patients according to age and sex

Age (in years)		Sex		Total
		Females	Males	
Under 20	number (N)	-	-	-
	%	-	-	-
21-30	number (N)	-	-	-
	%	-	-	-
31-40	number (N)	-	1	1
	%	-	7.70	4.67
41-50	number (N)	-	6	6
	%	-	46.15	28.57
Over 50	number (N)	8	6	14
	%	100	46.15	66.67
Number of patients		8	13	21

Chronic glomerulonephritis was the most frequent disease which brought to the CRF patients undergoing hemodialysis (43.34%), as shown in Table 4.

Table 4. Basic disease brings to the CRF patients undergoing chemodialysis

Disease	Number	%
Chronic glomerulonephritis	13	43.34
Unknown	7	23.34
Vesicoureteral reflux (VUR)	3	10.00
Polycystic kidney disease	2	6.67
Systemic Lupus erythematosus (SLE)	1	3.33
Diabetic nephropathy	1	3.33
Sy. Alport	1	3.33
IgA nephropathy	1	3.33
Nephroangiosclerosis	1	3.33
Total	30	100.00

The most frequent diseases in patients of the group 2 were: ventricular ulcers, (42.86%) and duodenal ulcer (28.57%), while erosions were found in 14.29% of the investigated patients as shown in Table 5.

In the group 1, erosions were found in 30% of patients, angiodysplasias in 6.67%, and ventricular polyp, duodenal ulcers, and ventricular ulcers in 3.33% as shown in Table 6. A regular endoscopic finding was present in 53.34% of patients (Table 6).

Table 5. Basic disease in the patients group 2

Disease	Number (N)	(%)
Ventricular ulcer	9	42.86
Duodenal ulcer	6	28.57
Erosions	3	14.29
Stomach neoplasm	1	4.76
Without disease	2	9.52
Total	21	100.00

Table 6. Endoscopic findings in the patients group 1

Endoscopic findings	Number (N)	(%)
Erosions	9	30.00
Ventricular polyps	1	3.33
Stomach neoplasm	–	–
Duodenal ulcers	1	3.33
Ventricular ulcers	1	3.33
Angiodysplasias	2	6.67
Without disease	16	53.34
Total	30	100.00

The endoscopic finding of erosions was present in all age groups, a bit more frequently in the group 41-50 years (10%).

Angiodysplasias were found only in patients of the age group over 50 years (3.33%). Ventricular ulcers and duodenal ulcers were found in the age group 41-50 years.

Erosions were detected in 10% of patients with chronic glomerulonephritis, and in 3.33% of patients with duodenal ulcers and ventricular ulcers. In patients with polycystic disease, erosions were detected in 6.67% of patients, while in patients with VUR, erosions were detected in 3.33% as well as in patients with nephroangiosclerosis, diabetic nephropathy, and unknown basic renal disease.

The most frequent endoscopic finding in patients of the group 2 were: ventricular ulcers (42.86%), duodenal ulcers (28.57%), and erosions (14.29%). In this group, the occurrence of stomach neoplasm was found in one patient (4.76%).

The greatest number of patients was undergoing dialysis for less than 4 years (53.33%). The occurrence of stomach polyps and duodenal ulcers was established in the first year of dialyzing. Erosions and ventricular ulcers were diagnosed after two years of dialyzing, while angiodysplasias were found in patients undergoing dialysis for the longest period, after 6.5 years.

The most frequent problems in patients of the group 1 were: loss of appetite (16.67%), nausea (16.67%), and vomiting (13.33%).

The most frequent problems in patients of the group 2 were: nausea (38.1%), vomiting (33.33%), and loss of appetite (28.57%).

A positive endoscopic finding was present in 14 patients with subjective problems.

A statistically significant difference was found in subjective problems in patients with endoscopic finding ( $p < 0.01$ ). The most frequent endoscopic finding in both investigated groups was the painful sensitivity of the epigastrium to deep palpation. In patients of the group 2, the painful sensitivity under the right rib arch was more fre-

quent, as well as a diffuse painful sensitivity of the stomach. However, the differences showed no statistical significance.

Endoscopic changes were found in patients of the group 1 who consumed alcohol, but the differences showed no statistical significance.

Endoscopic changes were more frequent in patients of the group 2 who consumed alcohol, but there was no statistically significant difference between the groups of patients.

Erosions were present in 40% of patients taking drugs, and only in 10% of patients not taking drugs. As much as 80% of patients not taking drugs had a regular endoscopic finding. A statistically significant difference was found in the patients of the group 1 with a regular endoscopic finding who were not taking drugs ( $p < 0.01$ ).

Endoscopic changes were a bit more frequent in the patients of the group 2 who were taking drugs, but differences were not statistically significant.

A statistically significant difference ( $p < 0.01$ ) was found in the patients of the group 1 who were cigarette consumers, and 70% of which had the endoscopic finding of erosions.

In the group 2 patients who were cigarette consumers, endoscopic changes were more frequent although there was no statistically significant difference.

## Discussion

Uremic patients frequently suffer from digestive problems, most frequent of which are nausea and vomiting, resulting from the accumulation of metabolic products of proteins.

The prevalence of gastro duodenal lesions and relevant gastrointestinal symptoms varies depending on whether they are uremic patients not undergoing dialysis, or patients undergoing dialysis, or patients with kidney transplantation. The incidence of gastrointestinal symptoms varies from 37% to 93% (3). According to the results obtained in our study, dyspeptic problems were detected in 46,6% of uremic patients undergoing dialysis.

The most frequent gastrointestinal symptoms in uremia are the consequence of disequilibria of liquid and electrolytes, mechanical, physical, and emotional problems of patients, and toxins which cannot be removed by dialysis and which cause abnormalities in stomach gastric emptying (4).

Several different mechanisms lead to the changes in the digestive tract in patients undergoing dialysis. The use of different drugs is associated with the changes in the digestive tract (5). The gastrin level is increased in patients with renal failure (6). The increase of gastrin may be partly explained by decreased renal metabolism of gastrin (7). Gastric acid secretion is very frequently decreased in these patients as a result of atrophic gastritis (8). It has been established that atrophic gastritis occurs in 15% of patients undergoing dialysis, while that percent in normal population amounts to only 2% (9).

It has been considered that gastrin not only increases gastric acid secretion but also influences the decrease in pyloric sphincter tone. The increased level of gastrin can reinforce both biliary reflux and damage of mucosa (10). The higher level of urea in patients undergoing dialysis can lead to the increase in proton diffusion in the gastrointestinal lumen (10). The increased bicarbonate secretion by the pancreas and increased pepsinogen synthesis (10) play a significant role in the appearance of duodenal lesions in renal failure.

The prevalence of peptic ulcers is very different and depends on the applied diagnostic methods (11). In our study, in the investigated group of patients undergoing dialysis, duodenal ulcers were detected in 3.33%, and ventricular ulcers in 3.33 % of patients as well. In the control group, duodenal ulcers were detected in 28.57 % and ventricular ulcers in 42.86% of patients.

The occurrence of erosions in patients undergoing chronic dialysis is conditioned by numerous factors; external factors such as alcohol consumption, use of glucocorticoids and nonsteroid antirheumatics, smoking cigarettes, various drug intake, non-observance of dietetic regime, play a significant role as well as stress situations and hormonal imbalance (11).

Several different studies pointed to the occurrence of erosive changes in about 50% of patients undergoing dialysis (11,12).

In our study, 30% of investigated uremic patients undergoing dialysis had erosive changes. Acute erosive changes were detected in 22.22%, and chronic in 77.78% of investigated patients. Erosions localized in the gastric antrum were found in 33.33%, and erosions in the duodenal bulb were detected in 66.67% of investigated patients.

In the control group, erosions were detected in 14.29% of patients.

The results obtained in our study conform with the results in the literature (11,12).

The basic therapy for peptic ulcers, as well as for erosive changes, consists of histamine 2 receptor blockers administered in a lower dose, depending on the severity of renal failure. Omeprazol is a potential drug for lowering gastric acid. It is very efficient in patients undergoing dialysis and does not require a dose lowering as the other proton pump inhibitors do (11,12).

Angiodysplasias are relatively frequent in uremic patients with the prevalence ranging from zero to 19-32% (13); in our investigation the prevalence was 6.67%. The use of heparin in patients undergoing chemodialysis increases and prolongs the eventual occurrence of bleeding from angiodysplasia. The main pathological mechanism is most probably multifactorial, where the key factors of vascular calcification are the imbalance in the calcium/phosphorus ratio, the severity of uremia, and a high-level of gastrin, parathormone and pepsinogen. Endoscopy and angiography are considered the only effective methods for establishing a diagnosis in patients with HBI (13,14).

It has been considered that endoscopy is a more efficient method, and that it is very efficient at establishing the diagnosis; further, it has been considered that the sensitivity of endoscopy is even higher in comparison with angiography (15). On those grounds, angiography is considered a complementary method when the endoscopic result is unreliable. In addition, endoscopy provides a unique possibility to be performed both in diagnostics and in therapeutic purposes during the same treatment (16). Endoscopic sclerostomization is a simple, cheap method, providing a possibility of repetition, and is relatively noninvasive.

A great number of studies reported a more frequent occurrence of angiodysplastic lesions in patients with severe uremia (17).

Our investigation points out the presence of angiodysplastic changes localized in the gastric antrum in two patients (6.67%), which conforms with the results reported in the literature by western authors (18).

So far, the occurrence of stomach polyp in patients with HBI undergoing chronic hemodialysis has not been reported in the literature (19). However, in the course of our investigation, we observed the case of one patient (3.33%) with polyp endoscopically confirmed.

In the patients included in our investigation, no erosive, prepyloric changes were observed which, according to literature were associated with the presence of uremia in investigated patients (19).

Uremic patients with or without digestive difficulties, have to undergo endoscopic examination periodically.

We consider that these patients should be treated prior to eventual kidney transplantation in case of any digestive disease presence.

## Conclusion

In patients undergoing chronic chemodialysis with digestive problems, and in transplantation balance, the performance of proximal endoscopy is recommended for prevention, detection, and future treatment of gastrointestinal disturbances.

Frequent digestive problems in patients undergoing chronic chemodialysis represent a compulsory indication for proximal endoscopy. Proximal endoscopy enables the prevention and diagnostics of gastrointestinal disorders. It is of particular significance in pretransplantation balance for the prevention from immunosuppressive therapy. By proximal endoscopy performed in patients undergoing chronic dialysis, the following pathological changes were confirmed: erosions in 9 (30%), angiodysplasias in 2 (6.67%), ventricular ulcers in 1 (3.33%), duodenal ulcers in 1 (3.33%), ventricular polyps in 1 (3.33%), and a regular finding was established in 16 (53.34%) patients. Confirmed changes in the gastrointestinal tract show that proximal endoscopy is a necessary method that should be used in patients undergoing chronic chemodialysis, particularly in the first years of dialyzing.

Proximal endoscopy enables diagnostics, early detection, monitoring the evolution and the effects of applied therapy, gastrointestinal disorders in patients un-

dergoing chronic chemodialysis in both pretransplantation balance and after kidney transplantation.

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## ENDOSKOPSKI NALAZ PROMENA SLUZOKOŽE PROKSIMALNOG DELA DIGESTIVNOG TRAKTA U BOLESNIKA SA HRONIČNOM BUBREŽNOM INSUFICIJENCIJOM NA HRONIČNOM PROGRAMU HEMODIJALIZE

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Kratak sadržaj: *Prospektivnom studijom je obuhvaćeno 30 bolesnika sa hroničnom bubrežnom insuficijencijom na hroničnom programu hemodijalize, sa ili bez digestivnih tegoba kod kojih je rađena proksimalna endoskopija u cilju pretransplantacionog bilansa u periodu od 1998. do 2000. godine. Studija je obuhvatila pacijente Instituta za nefrologiju i hemodijalizu Kliničkog centra u Nišu i pacijente Klinike za nefrologiju Kliničkog centra Srbije u Beogradu. Kontrolnu grupu čini 21 bolesnik bez hronične bubrežne insuficijencije koji su lečeni i ispitivani na Klinici za gastroenterologiju i hepatologiju Kliničkog centra Niš, kod kojih je rađena proksimalna endoskopija. Bolesnici su odabrani metodom slučajnog izbora. Proksimalnom endoskopijom u bolesnika na hroničnom programu hemodijalize verifikovali smo sledeće patološke promene: erozije u 9 (30%), angiodisplazije u 2 (6,67%), ulkus ventrikuli u 1 (3,33%), ulkus b. duodeni u 1 (3,33%), polipus ventrikuli u 1 (3,33%) i uredan nalaz u 16 bolesnika (53,34%). Spoljašnji faktori doprinose gastrointestinalnim promenama: konzumiranje umerene količine alkohola, pušenje cigareta, korišćenje raznih lekova, i nepridržavanje higijeno-dijetetskog režima. Ovi faktori rizika takođe doprinose u odlučivanju za primenu proksimalne endoskopije. Prisustvo subjektivnih tegoba od strane digestivnog trakta uz objektivni nalaz bolesnika na hroničnom programu hemodijalize čine indikaciju za proksimalnu endoskopiju a u cilju prevencije i ranog otkrivanja promena na digestivnom traktu. Indikacije za proksimalnu endoskopiju bolesnika na*

*hroničnom programu hemodijalize prema našim istraživanjima su: bolesnici u prvoj i drugoj godini dijaliziranja, učestale digestivne tegobe, a koje nisu u užoj vezi sa uremičkom intoksikacijom, akutna gastrointestinalna simptomatologija (bolovi u trbuhu, hematemeza, melena i dr.), pretransplantacioni bilans, i bolesnici sa hroničnim sistemskim oboljenjima, a primaju imunosupresivnu terapiju duže od 6 meseci.*

*Ključne reči: endoskopske promene, hemodijaliza, proksimalna endoskopija*