

## Upper Gastrointestinal Bleeding in Chronic Kidney Disease Patients

DANIELA MARINESCU<sup>1</sup>, M. LAZAR<sup>2</sup>, S. ZAHARIE<sup>3</sup>,  
COSMINA COMANESCU<sup>2</sup>, CLAUDIA TUDORAN<sup>2</sup>, M. BICA<sup>2,4</sup>, L. BARBU<sup>5</sup>

<sup>1</sup>University of Medicine and Pharmacy of Craiova

<sup>2</sup>Emergency Hospital of Craiova, 1<sup>st</sup> Surgical Clinic

<sup>3</sup>Emergency Hospital of Craiova, Nephrology Clinic

<sup>4</sup>University of Medicine and Pharmacy of Craiova, Department of Surgery

<sup>5</sup>University of Medicine and Pharmacy of Craiova, PHD fellow

**ABSTRACT:** **Aim:** To investigate upper GI bleeding as a particular complication in chronic kidney disease patients. **Material and method:** 30 chronic kidney disease patients admitted to the Nephrology Department for upper gastrointestinal bleeding over a period of 5 years. **Results:** 16 patients were undergoing hemodialysis (53.3%) and 14 patients were not in a hemodialysis program. There were no patients undergoing peritoneal dialysis. Very high comorbidity rate for all patients, most important being cardiovascular diseases. Only 10% of patients had oral anticoagulant treatment prior to GI bleeding. Conservative treatment was successful for all patients; no endoscopic or surgical haemostasis was needed. **Conclusion:** Although chronic disease kidney patients have a high risk of upper GI bleeding compared to the general population, the conservative treatment applied has a very high rate of success in stopping the bleeding without the need for endoscopic or surgical haemostasis treatment.

**KEYWORDS:** upper GI bleeding, chronic kidney disease, hemodialysis

### Introduction

Upper GI bleeding is a form of digestive tract hemorrhage manifesting as hematemesis and/or melena that has its source above the Treitz angle. The main cause of upper GI bleeding is gastro-duodenal ulcer, diagnosed in more than half of upper GI bleeding patients. H. Pylori has a defining role in the pathogeny of these ulcers but the chronic use of NSAID has also been incriminated. The second cause of upper GI bleeding is the esophageal varices in liver cirrhosis patients. The third most frequent cause of upper GI bleeding is represented by upper digestive tract tumors. [1-7]

Upper GI bleeding in chronic kidney disease patients represent a unique entity due to the many systemic physiopathological disorders that the renal disfunction creates much more complex than the urinary problems alone. The risk of upper GI bleeding in chronic kidney disease patient increases as the haemostasis disturbances induced by the renal disease are higher. The renal patient has a high risk of major bleeding due to platelets dysfunction with adhesion and aggregation alteration or low levels of platelet clotting factors and also due to increased capillary permeability and fragility specific to the renal patient. Variation of plasmatic levels of clotting factors, antithrombin and calcium are also associated. For end stage renal disease (ESRD) patients, clotting status alteration induced by dialysis are added. [8-12]

### Material and method

This is a retrospective descriptive study involving 30 chronic kidney disease patients admitted and treated for upper GI bleeding in the Nephrology Department between 2011-2015. We analysed the clinical charts of all patients. Comorbidities, clinical manifestations, degree of anemia, endoscopy findings and patients treatment were followed. The results were compared to studies in international literature.

### Results

There were 16 male patients representing 53.3% of cases and 14 female patients – 46.7%. urban patients represented 40% (12 patients) as rural patients were 60% (18 patients). The distribution of patients by age groups is presented in Table 1.

**Table 1. Age group distribution**

Age group	No.	%
31 - 40	2	6.7%
41 - 50	1	3.3%
51 - 60	6	20%
61 - 70	4	13.3%
Over 70	17	56.7%
Total	30	100%

The dialysis status of the patients in the study group is reflected in Table 2. There were 16 patients on dialysis representing 53.3%. 4 patients underwent dialysis using a central venous catheter (CVC) and 12 patients had an AVF (arterial-venous fistula). 14 patients were not on dialysis.

**Table 2. Dialysis status of patients**

Dialysis status		No.	%
On dialysis	Central Venous Catheter	4	13.3%
	Arterial-Venous Fistula	12	40%
Not on dialysis		14	46.7%
Total		30	100%

The different types of renal diseases encountered in the study group are presented in Table 3.

**Table 3. Renal diseases**

Renal disease	No.	%
Hypertensive nephropathy	7	23.4%
Chronic glomerulonephritis	9	30%
Chronic interstitial nephropathy	5	16.7%
Nephrotic syndrome	1	3.3%
Polycystic kidney	1	3.3%
Renal lithiasis	3	10%
Chronic pielonephritis	2	6.7%
Renal amiloidosis	1	3.3%
Hiperuricemic nephropathy	1	3.3%
Total	30	100%

Important comorbidities were registered in the study group. Diabetes was present in 8 cases (26.7%). 4 patients had obesity representing 13.3%. We noted hyperthyroidism in one case and secondary hyperparathyroidism in 2 cases. 2 patients had osteo-articular diseases while low plateles levels were present in 6 patients. There was one patient with a graft reject. Neurological disorders were encountered in 9 patients: 5 patients had post stroke sequelae while uraemic encephalopathy, cerebral lacunarism, Alzheimer's disease and peripheral neuropathy were present in one case each. Electrolyte levels disturbances were present in 23 patients, representing 76.6% of the group. Chronic hepatitis was noted in one case while cirrhosis of the liver was registered also in one case. 2 patients had chronic pulmonary diseases.

The most frequent comorbidities were represented by cardiac diseases. We registered the following groups of cardiac disorders:

1. Coronary disorders:
  - Acute myocardial infarction – 2 patients, 6.67%
  - Angina – 2 patients, 6.67%
  - Chronic Ischemic Cardiopathy – 3 patients, 10%
2. Arrhythmias
  - Atrial fibrillation – 7 patients, 23.3%
  - Right branch block – 1 patient, 3.3%
  - Left branch block – 1 patient, 3.3%
  - Tachycardia – 1 patient, 3.3%
  - Atrial-Ventricular block – 1 patient, 3.3%
  - Atrial flutter – 1 patient, 3.3%
3. Cardiopathy
  - Hypertensive cardiopathy – 4 patients, 13,3%
  - Hiperuremic cardiopathy – 2 patients, 6,6%
  - Dilative cardiomiopathy – 1 patient, 3,3%
  - Mixed cardiopathy – 2 patients, 6,6%
  - Left ventricle failure – 1 patient, 3,3%
4. Cardio-vascular diseases
  - Hypertension – 23 patients, 76.7%
  - Chronic cardiac failure – 13 patients, 43.3%
  - Chronic venous disease – 2 patients, 6.6%
  - Arterial peripheral disease – 2 patients, 6.6%

Regarding medication of patients before the GI bleeding episode, only 3 patients (10%) received anticoagulants. No patient had anti-inflammatory treatment before the GI bleeding.

The clinical expression of the upper GI bleeding was as follows: 21 cases only presented with melena (70%), 4 patients only had hematemesis (13.3%) while 5 patients were admitted with both hematemesis and melena (16.7%). This data is illustrated in Table 4.

**Table 4. Clinical expression of UGIB**

Clinical expression	No.	%
Melena	21	70%
Hematemesis	4	13.3%
Melena and hematemesis	5	16.7%
Total	30	100%

The clinical manifestation of upper GI bleeding was mild for most patients. 24 patients (80%) presented with a blood pressure (BP) higher than 100/60mmHg and a heart rate (HR) under 100b/min. 6 patients (20%) presented with BP lower than 100/60mmHg and HR higher than 100b/min but these values normalized after beginning of treatment.

Anemia was present for all patients. The different degrees of anemia registered in the study group are presented in Table 5.

**Table 5. Grades of anemia**

Hb	No. of patients	%
>10g/dl	6	20%
8-10g/dl	10	33.3%
5-8g/dl	8	26.7%
<5g/dl	6	20%
Total	30	100%

Conservative treatment was applied for all patients. Haemostatic treatment was administered to all 30 patients (100%). 73.3% of patients received PPI whereas the other 26.7% were treated with anti H2 medication. Antiacids were given to all 30 patients.

Endoscopy was performed for only 5 patients. The results were: erosive gastritis, erosive gastro-duodenitis and duodenal bleeding ulcer for 1 patient each. Two patients did not have any lesions visible during endoscopy.

**Discussion**

We studied a group of 30 CKD patients, 16 patients undergo hemodialysis, 14 patients without hemodialysis. No upper GI bleeding was recorded in peritoneal dialysis patients as these patients are prone to mechanical and infectious complications. It is important to note the low number of upper GI bleeding cases (30 patients) over a fairly long period of time.

As the chronic renal disease sex incidence is equal for men and women, the sex incidence for upper GI bleeding in renal patients is similar for men and women. Also, patient's background is not a risk factor for GI bleeding. Age group is directly proportional to the risk of bleeding in renal patients, as seen in our study group. GI bleeding was encountered in both hemodialysis and non-hemodialysis patients. No patients were undergoing peritoneal dialysis. A higher risk of GI bleeding can be observed for dialysis patients compared to patients without renal function substitution. In the group of hemodialysis

patients, most have an arterial-venous fistula (AVF) angioaccess. These are patients with long term dialysis as opposed to a central venous catheter (CVC) that is used mostly for emergencies. [13]

Studies show that patients with a GFR of 30ml/min have a major bleeding risk 4.3 times higher. In end stage renal disease (ESRD) patients the risk of upper GI bleeding (UGIB) is 1.4 – 5.2 times higher compared to non chronic kidney disease (CKD) patients but lower than the risk of cerebral bleeding that is 6 – 10 times higher. [14]

It is a known fact that CKD patients have a significant risk of blood clotting disorder due to altered nitrous oxide (NO) metabolism and uraemic toxemia. [14]

The association of diabetes for ESRD patients carries a high risk of bleeding due to altered coagulation caused by glycozilation and also due to microvascular lesions specific to diabetes patients. This explains the high frequency of diabetes patients in our CKD and UGIB group.

A similar situation can be seen regarding the high rate of cardiovascular diseases in our study group. The high risk of UGIB for these patients is due to ischemic status in the gastro-intestinal tract. Cardiovascular morbidity can be correlated to blood vessels aging, much accelerated in renal patients for which biological age is far bigger than chronological age compared to non CKD patients. This phenomenon is also associated with the role of epithelial tube cells in producing anti-aging proteins. [15]

In our study, we had patients with graft reject that developed UGIB but no patients with viable kidney transplant. As for the peritoneal dialysis patients, our findings are consistent with literature data that associates a very low risk of UGIB in kidney transplant patients and peritoneal dialysis patients.

We found a high incidence of arrhythmias in our study group. Studies in literature show that Atrial Fibrillation (AFi) has a 11.6% rate in ESRD patients. AFi high rate is associated with age, males, Caucasians, long history of ESRD and dialysis as well as the presence of cardiac, vascular, coronary, cerebrovascular or perriferal arterial diseases. [16]

The risk of stroke in dialysis patients is 2% but it increases to 5% if AFi is associated. As a result, the opportunity of oral anticoagulant treatment can be discussed. Patients with low GFR have a vitamin K deficit and adding oral anticoagulants in their treatment can increase the

risk of bleeding. Also, oral anticoagulants inhibit the synthesis of a protein that inhibits the process of calciphylaxis. As a result the vascular disease of dialysis patients in chronic treatment with oral anticoagulants progresses and the risk of bleeding increases directly proportional with disfunction and structural vascular alteration. [14, 16]

Other studies show an AFI risk 3 times higher in CKD patients compared to non-CKD patients. [14]

The risk of thrombo-embolic events increases along with the decrease of GFR even if AFI is absent. Cases of spontaneous formation of thrombi in the left atrial appendage in dialysis patients are described in many studies. This leads to a debatable indication of oral anticoagulants in CKD patients. [16]

Chronic kidney disease uremic/non-uremic stage is associated with some degree of anemia. Patients receive iron medication and erythropoietin. Due to the fact that patients tend to adjust to the anemia, the correlation between the severity of the anemia and the gravity of the UGIB is less relevant than it is for non CKD patients. [10, 12]

Differentiating the CKD secondary anemia – normochromic, normal red blood cells, caused by erithropoetin deficit –from post bleeding hypochromic anemia is done using biochemical tests: hemoglobin, hematocrit, reticulocytes, ferritin, hemolysis markers and peripheral blood smear. This is important in correlating the gravity of anemia with the gravity of UGIB. [10, 12]

Literature states that erosive gastritis is 6 times more frequent in ESRD patients compared to normal population. The diagnosis is established during endoscopy but no hemostasis procedure can be applied due to the diffuse nature of bleeding. [12]

In our study group there were only 2 patients with erosive gastritis or gastro-duodenitis. This is due to the fact that only 16.7% of cases underwent an endoscopic exploration. The real number of gastritis cases is probably much higher.

Although studies show that angiodisplasia is a frequent cause of UGIB in ESRD patients, we found no such case in our study group. For more than 90% of cases with angiodisplasia, the bleeding stops spontaneously. This can explain the absence of such cases in our study group.

A rare cause of UGIB in CKD and ESRD patients, as described in literature, is a condition called “watermelon stomach” – a localized form

of angiodysplasia confined to the gastric antrum that responds well to oestrogen-progesterone therapy. [17] We found no such case in patients that underwent endoscopy.

Studies show that UGIB in CD patients presents usually with mild clinical manifestations and responds well to conservative treatment.[18] In our study all patients received haemostatic medication, with a fair outcome. There was no need for endoscopic or surgical haemostasis. Despite the presence of cirrhosis patients in the group, no vasopressin or somatostatin analogs were used.

For all hemorrhagic events in CKD patients undergoing dialysis, a “heparin free dialysis” is instated until the bleeding stops. Subsequently, increasing dosage of anticoagulant is resumed during dialysis. [8]

## Conclusion

UGIB has a high rate of occurrence in CKD patients but usually presents with mild clinical manifestations and has a fair outcome with conservative treatment, no endoscopic or surgical haemostasis being needed.

## References

1. Irinel Popescu sub red. *Tratat de Chirurgie*. Vol. VIII Partea 1B – Chirurgie Generala. Ed Academiei Romane, Bucuresti, 2008
2. Ion Georgescu sub red. *Chirurgie Generala*. Curs Universitar. Ed Universitara Carol Davila, Bucuresti, 2015
3. Fane Ghelase sub red. *Chirurgie*. Patologie Chirurgicala. Vol. III. Sitech, Craiova, 2013
4. Leclaire S, Di Fiore F, Merle V, Herve S, Duhamel C, Rudelli A, et al. Acute upper gastrointestinal bleeding in patients with liver cirrhosis and in noncirrhotic patients: epidemiology and predictive factors of mortality in a prospective multicenter population-based study. *J. Clin. Gastroenterol*. 2005;39(4):321-7.
5. Wilcox CM, Alexander LN, Cotsonis G. A prospective characterization of upper gastrointestinal hemorrhage presenting with hematochezia. *Am j Gastroenterol* 1997;92(2):231-5.
6. C. H. Morales-Urbe<sup>1</sup>, S. Sierra-Sierra<sup>2</sup>, A. M. Hernández-Hernández<sup>2</sup>, A. F. Arango Durango<sup>2</sup> and G. A. Lopez<sup>2</sup> Upper gastrointestinal bleeding: risk factors for mortality in two urban centers in Latin America. *REV ESP ENFERM DIG (Madrid)* 2011, 103(1):20-24
7. Farrell jj, Friedman LS. The management of lower gastrointestinal bleeding. *Aliment Pharmacol Ther* 2005;21(11):1281-98.
8. Jenny I Shen, Aya A Mitani, Tara I Chang and Wolfgang C Winkelmayer. Use and safety of heparin-free maintenance hemodialysis in the USA. *Nephrol Dial Transplant* (2013) 28: 1589-1602 doi: 10.1093/ndt/gft067

9. Pei-Chen Wu and Vin-Cent Wu. Long term risk of upper gastrointestinal hemorrhage after advanced acute kidney injury: a population-based case-control study. *Nephrology Dialysis Transplantation* 29 (supplement 3): iii102-iii113, 2014, SP112. doi: 10.1093/ndt/gfu144
10. Nicolae Ursea. *Tratat de Nefrologie. Vol. 2 Rinichi si tulburari de coagulare.* CID. Ed Fundatia Romana a Rinichiului, 2006.
11. Alexandru Ciocalteu. *Tratat de Nefrologie.* Ed National Bucuresti, 2006
12. Adrian Covrig. *Nefrologie. Principii teoretice si practice.* Casa Editorial Demiurg, Iasi, 2011.
13. Haimanot Wasse, Daniel L Gillen, Adrienne M Ball, Bryan R Kestenbaum, Sthephen L Seliger, Donald Sherard and Catherine O Stehman-Breen. Risk factors for upper gastrointestinal bleeding among end-stage renal disease patients. *Kidney International*, vol. 64 (2003), pp. 1455-1461
14. Thilo Kruger, Vincent Brandenburg, Georg Schlieper, Nikolaus Marx and Jurgen Floege. Sailing between Scylla and Charybdis: oral long-term anticoagulation in dialysis patients. *Nephrol Dial Transplant* (2013) 28: 534-541 doi: 10.1093/ndt/gfs485
15. Giuseppe Castellano, Angelica Intini, Alessandra Stasi, Chiara Divella, Paola Pontrelli, Margherita Gigante, Anna Zito, Giovanni Batista Pertosa, Loreto Gesualdo and Giuseppe Grandaliano. Modulation of anti-ageing KLOTHO (KL) in patients with delayed graft function and ischemia/reperfusion injury: possible role of complement in the regulation of transplant cellular senescence. *Nephrology Dialysis Transplantation* 29 (supplement 3): iii102-iii113, 2014, SP106. doi: 10.1093/ndt/gfu144
16. Catherine M Clase, Rachel M Holden, Manish M Sood, Claudio Rigatto, Louise M Moist, Benjamin KA Thomson, Johannes FE Mann and Deborah L Zimmerman. Should patients with advanced chronic kidney disease and atrial fibrillation receive chronic anticoagulation? *Nephrol Dial Transplant* (2012) 27: 3719-3724 doi: 10.1093/ndt/gfs346
17. C Hermans, E Goffin, Y Horsmans, E Laterre and Ch Van Ypersele de Strihou. Watermelon stomach. An unusual cause of recurrent upper GI tract bleeding in the uraemic patient: efficient treatment with oestrogen-progesterone therapy. *Nephrol Dial Transplant* (1996) 11: 871-874
18. Miso Sabovic, Janez Lavre and Bojan Vujkovic. Tranexamic acid is beneficial as adjunctive therapy in treating major upper gastrointestinal bleeding in dialysis patients. *Nephrol Dial Transplant* (2003) 18: 1388-1391 doi: 10.1093/ndt/gfg117

---

*Corresponding Author: Bica Marius, 1st Surgical Clinic Emergency Hospital of Craiova, Str Tabaci nr 1, Craiova, Dolj; e-mail: mariusbk@yahoo.com*