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Medical causes of acute kidney injury- clinical and therapeutic aspects in constanta county

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ABSTRACT.

Introduction. Acute kidney injury represents an important clinical syndrome within nephrology, approximately 5% of hospitalised patients being affected. Establishing a diagnosis for acute kidney injury can be challenging and requires many steps. A complete and correct diagnosis is essential for appropriate therapy and, ultimately, the patient's prognosis.

Methods. An objective of this study is to determine the presentation of certain characteristics for the diagnosis of acute kidney injury. It is also intended to show the therapeutic methods undertaken for patients presenting with acute kidney injury, as well as evolution under therapy.

Results. The most common causes of acute kidney injury were medical causes and within that category, cardiovascular diseases were the most common etiological factor (18%). Nephropathies represented a minority, with acute pyelonephritis, responsible for 5% of medical causes, and acute glomerulonephritis accounting for 6%. Hemodialysis was initiated only in 15% of patients. The rest of the patients were treated conservatively and responded favourably to this therapeutic approach. The etiological factors that had the greatest number of patients requiring hemodialysis were Rifampicin administration and leptospirosis (~20% each).

Conclusions. The clinical characteristics of acute kidney injury are variable and are usually specific to the etiology of the disease. The most common causes were cardiovascular diseases (18%). The therapeutic

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145, Tomis Bvd, Emergency Clinical County Hospiatal of Constanta, Nephrology Department e-mail: tutaliliana@yahoo.com telephone: +40722300505 fax number: +40241662070 approach was rather conservative. Hemodialysis was instituted only in 15% of the patients. Almost 5% of all patients evolved to chronic kidney disease in a variable period of time, and the overall mortality was 18%, mainly due to infections and cardiovascular complications.

Key words: Acute kidney injury, dialysis, conservative therapy, chronic kidney disease

Introduction

Acute kidney injury (previously referred to as Acute renal failure) represents an important clinical syndrome within nephrology. Western European studies show that approximately 5% of hospitalised patients are affected by acute kidney injury.

Multiple definitions have until recently been used for acute kidney injury (AKI), formerly and therefore the wide variation in definitions has made it difficult to compare results across studies and populations. Establishing a diagnosis for acute kidney injury can be challenging and requires many steps. A complete and correct diagnosis is essential for deciding on a correct course of therapy and ultimately the patient's prognosis. The relatively new Acute Kidney Injury Network (AKIN) criteria showed sensitivity and specificity in different studies, usually done for intensive care units (ICU) patients. [1].

Definition and staging of AKI are based on the Risk, Injury, Failure; Loss, End-Stage Renal Disease (RIFLE) and Acute Kidney Injury Network (AKIN) criteria and studies on risk relationships. [2].

AKI is defined as any of the following (Not Graded):

• Increase in SCr by X0.3 mg/dl (X26.5 lmol/l) within 48 hours; or

• Increase in SCr toX1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or

• Urine volume o0.5 ml/kg/h for 6 hours.

This classification system includes separate criteria for creatinine and urine output. A patient can fulfill the criteria through changes in serum creatinine or changes in urine output, or both. The criteria that lead to the worst possible classification should be used (Table I) [3].

Table I. RIFLE and AKIN classifications

Stage	Serum creatinine	Urine output
1	1.5-1.9 times baseline	
	OR	
	X0.3 mg/dl (X26.5 mmol/l) increase	0.5 ml/kg/h for 6-12 hours
2	2.0–2.9 times baseline	0.5 ml/kg/h for X12 hours
3	3.0 times baseline	0.3 ml/kg/h for X24 hours
	OR	OR
	Increase in serum creatinine to X 4.0 mg/dl	Anuria for > 12 hours
	OR	
	Need for renal replacement therapy	

This new staging system differs from the RIFLE classification as follows: it reduces the need for baseline creatinine but does require at least two creatinine values within 48 hours; AKI is defined as an abrupt (within 48 hours) reduction in kidney function, currently defined as an absolute increase in serum creatinine ≥ 0.3 mg/dl (≥ 26.4 µmol/l), a percentage increase in serum creatinine \geq 50% (1.5fold from baseline), or a reduction in urine output (documented oliguria < 0.5 ml/kg/hour for > 6 hours); risk maps to Stage 1, but it also considers an increase in serum creatinine $\geq 0.3 \text{ mg/dl}$ ($\geq 26.4 \mu \text{mol/l}$); injury and failure map to Stages 2 and 3, respectively; Stage 3 also includes patients who need renal replacement therapy irrespective of the stage they are in at the time of renal replacement therapy; and the two outcome classes loss and end-stage kidney disease have been removed. [3].

Aim of the Study

The objective of this study was to determine the presentation of certain characteristics for the diagnosis of acute kidney injury. It is also intended to show the therapeutic methods undertaken for patients presenting with acute kidney injury, as well as evolution under therapy.

Material and Methods

A study was conducted using patients admitted January 1st 2011 – December 31st 2011 with acute kidney injury, with different medical etiologies, in the Emergency Clinical County Hospital, Nephrology Department. The cases also included patients from other clinical departments, like Cardiology, Neurology, Oncology, Intensive care unit, which requested a nephrology consultation for this clinical syndrome. Acute renal injury was defined as an acute deterioration of renal function, with a sharp increase of serum creatinine (> 2mg/dl) in patients with a previously normal renal function.

Patients had either oliguric acute kidney injury (urine output of 100-400 ml/24 hours) or non-oliguric kidney injury (urine output > 400 ml/24 hours).

The diagnosis of the 604 patients studied was based on patient history, physical examination, clinical symptoms and paraclinical evaluation.

Data from patient history:

- Age
- Development of diuresis (sudden anuria or progressive reduction)
- Pre-existing renal disease
- Systemic disease with renal repercussions (e.g. diabetes mellitus)
- Severe cardiac insufficiency
- Volume depletion
- · Previous examinations with contrast substances
- Administration of nephrotoxic drugs (e.g. ACEinhibitors, NSAIDs)

Clinical considerations of an acute uremic syndrome were noted as diagnostic elements:

- Tenderness on palpation of the hypogastrium indicating a palpable urinary bladder obstruction
- Tenderness on palpation of the upper abdominal area suspicion of a ureteral obstruction or renal infarction
- Ascites suggestive of hepatic cirrhosis, nephrotic syndrome, Budd-Chiari syndrome
- · Abdominal breathing atherosclerotic disease

Paraclinical investigations:

- Complete blood count
- Urine examination including urinary sediment
- Biochemical tests urea, creatinine, uric acid, electrolytes, liver enzymes, coagulation factors
- · Renal ultrasound

Indications for the initiation of dialysis were:

- Severe hyperhydration
- Hyperkalemia (≥ 7mmol/l)
- Severe uraemia (> 250mg%)
- Severe metabolic acidosis (bicarbonates ≤ 7mEq/l)
- Severe, hypo- or hypernatremia
- Uremic pericarditis

Statistical analysis

Continuous variables are expressed as the mean \pm standard deviation, and categorical variables are presented as the percentage of the number of cases. Comparisons between RIFLE classes or AKIN stages were performed using analysis of variance and the chi-square test for continuous variables and categorical variables, respectively. Data are presented as odds ratios (ORs) with 95% confidence intervals (CIs). A two-tailed P value < 0.05 was considered significant. Analysis was performed with the statistical software package SPSS 15.0 for Windows.

Results

After examination of the relevant data for the 604 patients (62% males), the results obtained regarding acute kidney injury are presented below.

DISTRIBUTION OF PATIENTS BY AGE

Patients were aged 18-87 years old. Table 2 reveals a high incidence of acute kidney injury in middle aged patients. The two greatest incidences were in the age groups of 40-50 years and 50-60 years, with 28% and 24%, respectively (Table II).

Table II.	Distribution	of	patients	by	age	groups
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Age groups	Number of	Percentage (%)
	patients	
18-20	22	3
20-30	78	13
30-40	66	11
40-50	144	24
50-60	118	20
60-70	84	14
70-80	68	11
> 80	24	4
TOTAL	604	100

CLINICAL AND PARACLINICAL MANIFESTATIONS

From the 604 patients evaluated, 248 patients presented with non-oliguric acute kidney injury (urine output of < 400ml/24 hours). This figure represents acute kidney injury with a preserved diuresis. This could indicate a pre-renal acute kidney injury due to compensation of the hemodynamics and hydroelectrolyte balanceas seen in Table III.

Table III.	Clinical	presentation with regard to diuresis	

Type of acute kidney injury (diuresis)	Number of patients	Percentage (%)
Oliguric	356	59
Non-oliguric	248	41
TOTAL	604	100

Paraclinical data:

The most common biochemical modifications are shown in Table IV.

Table IV. Biochemical modifications on paraclinical

Laboratory data	Number of patients	Percentage from total patients (%)
Seric Urea > 100mg/dl	568	94
Seric Creatinine > 2mg/dl	556	92
Severe anemia	173	29
Hyperkalemia	354	59
Hypokalemia	227	38
Metabolic acidosis	239	40
Hypocalcemia	396	66
Hypernatremia	278	46
Hyponatremia	289	48

ETIOLOGICAL CLASSIFICATION

The etiology of acute kidney injury was divided into 3 groups: medical, surgical and obstetrical causes, as shown in Table V.

Table V. Causes of acute kidney injury in admitted

patients				
Causes	Number of patients	Percentage (%)		
Medical	362	60		
Surgical	206	34		
Obstetrical	36	6		
TOTAL	604	100		

Medical cases represented the vast majority of causes in admitted patients. These cases included a variety of sub-etiologies including volume loss, nephrotoxic drugs, nephrotoxic substances, sepsis etc.

The surgical cases included obstruction (lithiasis, benign prostatic hyperplasia, and neoplasias), post-operative pre-renal acute kidney injury, and trauma with or without rhabdomyolysis.

The obstetrical cases included septic abortion, haemorrhagic shock, postpartum sepsis, preeclampsia/eclampsia, idiopathic postpartum acute kidney injury.

MEDICAL CAUSES OF ACUTE KIDNEY INJURY

The most frequent causes of acute kidney injury that were of medical etiology were: fluid loss due to gastrointestinal reasons (diarrhea, haemorrhage), nephrotoxic drugs (aminoglycosides, contrast substances, NSAIDs), sepsis, other nephrotoxic substances (carbon tetrachloride, ethylene glycol), other unknown substances, acute tubulointerstitial nephropathy; both infectious and obstructive caused by endogenous substances (hemoglobin, myoglobin, uric acid). (Table VI)

Table VI. Medical causes of	°acute kidney injury in
admitted pa	itients

Medical causes	Number of patients	Percentage (%)
Cardiovascular	66	18
Nephrotoxic drugs/	54	15
substances		
Sepsis	45	12
Gastrointestinal fluid loss	50	14
Leptospirosis	28	8
Rifampicin	22	6
Acute glomerulonephritis	21	6
Acute pyelonephritis	18	5
Other causes	19	6
Unknown	39	10
TOTAL	362	100

In comparison with studies conducted in other regions in Romania, there is an increased incidence of acute kidney injury due to administration of Rifampicin, 15 cases for tuberculosis and 7 cases administered for dental or ENT infections. Hepatotoxicity was associated with 3 cases, in association with chronic alcoholism and malnutrition. Around 60% of patients with acute kidney injury due to the administration of Rifampicin require hemodialysis[4].

Severe acute kidney injury was due to leptospirosis was diagnosed in 28 cases (~8%). All of these cases were transferred from the Infectious Diseases hospital and indicates an increased incidence of this disease in this region.

The evolution of patients due to acute kidney injury due to medical causes is favourable under conservative treatment. However, in 20% of the cases, hemodialysis was necessary in order to resume diuresis.

TREATMENT IN MEDICAL CAUSES OF ACUTE KIDNEY INJURY

Conservative treatment options are defined as supportive therapy for the patient including the most important roles of balancing the fluid (volume expansion if necessary), correcting haematological abnormalities and balancing of electrolytes. (Table VII)

TREATMENT	NUMBER OF PATIENTS	percentage (%)
Haemodialysis	73	20
Conservative	289	80
TOTAL	362	100

Table VII. Therapeutical approach in medical causes of acute kidnev injury

HEMODIALYSIS IN ACUTE KIDNEY INJURY

As therapy for substitution of renal function, acute hemodialysis was performed in 73 patients, (20% of all medical cause AKI patients), even though the total number should have been greater. Unfortunately, due to late referral to Nephrology or to the dialysis centre, many patients died without starting dialysis.

Cases that underwent acute hemodialysis had the following etiologies, as shown in Table VIII.

Table VIII. Etiologies	that required he	modialysis

Causes	Number of	%
	patients	
Rifampicine	18	19,7
Leptospirosis	18	19,7
Intoxications	14	15,3
Nephrotoxic drugs	11	12
Other sepsis	6	6,5
Cancer	2	2,1
Post-transfusional hemolysis	1	1,1
Malaria	1	1,1
Unknown	4	4,3
Total	73	100

The most frequent conditions that underwent hemodialysis were: leptospirosis, Rifampicin administration for tuberculosis therapy, septic shock and acute intoxications/ nephrotoxic drugs.

DURATION OF HOSPITALISATION

The average length of stay was variable, generally being determined by the initiation of hemodialysis or fatal complications.(Table IX)

Table IX.	Duration	of hos	pitalisation

Patients	Duration of AKI	Duration of
	(days)	hospitalisation (days)
All patients	8,5 ± 10,4	20,9 ± 14,5
Survivors	$8,4 \pm 9,9$	$21,1 \pm 14,5$
Dialysed patients	$12,5 \pm 11,8$	$25,3 \pm 15,5$
Undialysed patients	4,3 ± 6,2	$16,3 \pm 12,6$
(unknown evolution)		

MORTALITY IN CONSERVATIVE TREATMENT

Death occurred in 71 patients out of 362. This represents a percentage of 18% mortality in therapy with conservative methods.

The cause of death in these patients is listed in Table X .

Table X. Causes of death in patients treated conservatively

Cause of death	Number of patients	Percentage (%)
Toxic/septic shock	16	19
Acute pulmonary oedema	20	24
Arrhythmias	14	17
Cardiovascular accidents	8	10
Multi-organ failure	11	13
Unknown	2	3
TOTAL	71	100

OVERALL MORTALITY

A total of 110 patients died of the 604 patients admitted for acute kidney injury. That represents an overall mortality of 18%.

EVOLUTION TO CHRONIC KIDNEY DISEASE

In 30 cases (4.96%), patients developed chronic kidney disease in a variable interval of time (1-5 years). They will enter, or have already started chronic hemodialysis.

Conclusions

The clinical characteristics for acute kidney are variable and are usually specific to the etiology of the disease.

The biochemical characteristics which are strongly suggestive of acute kidney injury are a rise in serum creatinine (>2mg/dl) and in serum urea (> 100mg%).

The most common cause of acute kidney injury was medical, within which, cardio-vascular diseases was the leading etiological factor, representing 18%.

The therapeutic approach for the majority of patients presenting with acute kidney injury was mainly supportive, hemodialysis been initiated in a small percentage of cases, ~15%.

The diagnostic criteria which determine the initiation of hemodialysis therapy are: severe hyperhydration, hyperkalemia (\geq 7mmol/l), severe uremia (urea \geq 250mg%; creatinine \geq 10mg%), metabolic acidosis (bicarbonates \leq 7mEq/l), hyper/ hyponatremia and uremic pericarditis.

The etiological factors that had the greatest number of patients requiring hemodialysis were Rifampicine administration and leptospirosis, both with $\sim 20\%$ each.

 \sim 5% of all patients evolved to chronic kidney disease in a variable period of time (3months- 2 years) and overall mortality was 18%.

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