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Epidemiology of acute kidney injury in Moroccan medical intensive care patients: A regional prospective, observational study

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Abstract: Objective: To evaluate the incidence, mortality and influencing factors for the development of Acute Kidney Injury (AKI) at admission or during Intensive Care Unit (ICU) stay. Methods: We conducted a prospective, epidemiological survey, in ICU for two years and the data of 97 patients admitted to ICU for medical illness was analyzed. Patients with AKI were categorized by serum creatinine and urine output into 3 stages. Stage 1 was defined as an absolute increase (within 48 hours) in serum creatinine of more than or equal to 0.3 mg/dl, or oliguria of less than 0.5ml/kg per hour for more than six hours. Stage 2 was defined as doubling of serum creatinine, or a urinary output lower than 0.5ml/kg /h for 12 h. Stage 3 was defined as tripling of serum creatinine or a urinary output lower than 0.3 ml/kg/h for 24 h, or anuria for 12 h. Results: Sixty patients (62 %) had AKI. AKI patients tended to be older and usually had antecedent of heart disease, a high Simplified Acute Physiology Score version II at admission, more use of mechanical ventilation and vasopressor treatment, more shock, more severe sepsis, more hyperosmolar hyperglycemic state (HHS) and higher mortality. In multivariate analysis, SAPS II score >30, antecedent of heart disease and shock were independent risk factors for development of AKI at admission or during ICU stay. Conclusion: AKI had a high incidence and a high mortality in medical ICU's patients. Antecedent of severe underlying diseases, heart disease and hemodynamic failure were independent risk factors of AKI.

Keywords: Acute Kidney Injury, Intensive Care Unit, Mortality, Risk Factors

1. Introduction

The incidence and mortality of acute kidney injury (AKI) continues to rise during hospital admission.[1-6] The variety of definitions used in clinical studies may be partially responsible for the large variations in the reported incidence and the associated mortality of AKI.[7-10] There was no controlled data about the epidemiology of AKI in medical critically ill patients in our regional hospital. Aims of our study were to evaluate the incidence, mortality and influencing factors for the development of AKI at admission or during ICU stay, and to compare the findings to the international experience.

2. Methods

2.1. Study Participants

This study was a prospective, epidemiological survey of AKI in medical ICU patients in a regional hospital in Morocco. The demographic, morbidity and outcome data of 97 adults patients admitted to ICU for sever medical illness between January 1st, 2010 and February 17th, 2012 was

analyzed. The participating centre is a regional hospital having access to a polyvalent intensive care unit with 6 beds. During the two years of the study, every newly patient admitted to ICU for medical illness was registered and was followed up until intensive care discharge or death in ICU.

Serum creatinine was determined and urine output was recorded for all patients every day. AKI was classified in three stages. Stage 1 was defined as an abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg/h for more than six hours). Stage 2 was defined as doubling of serum creatinine, or a urinary output lower than 0.5 ml/kg /h for 12 h. Stage 3 was defined as tripling of serum creatinine or a urinary output lower than 0.3 ml/kg/h for 24 h, or anuria for 12 h.

Patients were categorized by serum creatinine and/or urine output into the AKI stages and the highest AKI stage during ICU staying was evaluated. Serum creatinine on ICU admission was used as a reference value. Chronic kidney disease patients on dialysis (n = 9) were excluded from the analysis.

2.2. Data Collection

The Simplified Acute Physiology Score version II (SAPS II) was calculated based on the worst variables recorded during the first 24 hours of ICU admission.[11] Multiple data were collected on each study participant, including: demographics, co-morbidities, hospital and ICU admission and discharge data, presumed etiologies of AKI, renal replacement treatment modalities and outcomes.

Etiologies of AKI were identified from a group of six possible choices (shock: septic shock, hypovolemia, cardiogenic shock (these definitions were based on international guidelines), severe sepsis, hyperosmolar hyperglycemic state (HHS) and drug-induced nephrotoxicity (DIN).

We were asked to complete the data entry. Upon arrival, all data were screened in detail by a dedicated intensive care specialist for any missing information, insufficient detail, or any other queries. Any queries planned resolution within 48 h.

2.3. Statistical Analysis

All values were presented as mean values ± SD or as median with interquartile range (IQR) as appropriate. Qualitative variables were compared by the Chi Square 2 test or the Fisher test. Quantitative variables were compared with t test or Mann and Whitney test. A logistic regression analysis was performed to determine the independent risk factors for AKI. All variables were deemed to be significant if $p < 0.05$. All analysis was performed by the SPSS statistical software package 13.0.

3. Results

Altogether 97 patients (aged 56 years [29 – 69 years], male/female ratio: 55/42) were entered into the study. Baseline characteristics of the patients are summarized in Table 1.

At admission, 51% of patients had normal urea level, 76% had normal serum creatinine level and 49 % had normal serum creatinine and urea level. The incidence of AKI during intensive care stay was 62 % (n = 60). Forty-seven patients (48%) were in Stage 1, 12 patients (13 %) in Stage 2 and 1 patient (1%) in Stage 3. The major reason for ICU admission was disturbances of consciousness in 71% of cases, followed by respiratory distress in 48% of cases and shock in 20% of cases.

Antecedents, reason of ICU admissions and etiologies of AKI are summarized in Table 2. One patient received renal replacement therapy with a veno-venous technique and had AKI Stage 3. The overall utilization of intermittent renal replacement therapy was low 2 % of all AKI. The incidence of global mortality was 36%. The Mortality in patients with AKI was significantly higher than mortality in patients without AKI (52 % vs 11%. P<0.001). There was no different significative between the median of length of stay at the ICU in patients with AKI, vs patients without AKI (Table 3). AKI patients seem to be older (60 vs 34. years, p =0.,001) and usually had more severe underlying diseases (SAPS II 35 vs 18. p<0.001).

Independent risk factors for development of AKI evaluated by multivariate analysis were: SAPSII > 30, history of heart disease and shock (Table 4).

Table 1. *Characteristics of patients during ICU staying*

Parameters	All patient	AKI	non-AKI	p-AKI vs.non-AKI
Patient number, n (%)	97 (100)	60 (62)	37 (38)	
Age (years), median (IQR)	56 [29 - 68]	60 [47-71]	34 [22-60]	0.001
SAPS II. Score, median (IQR)	27 [18-39]	35 [24-45]	18 [12 -22]	< 0.001
Se-creatinine at ICU admission (MG/L), median (IQR)	10 [9-13]	12 [10-22]	10 [7-11]	< 0.001
Se-creatinine peak-concentration (MG/L), median (IQR)	11 [9-16]	13 [10-25]	10 [7-11]	< 0.001
Mechanical ventilation, n (%)	38 (39)	31 (32)	7 (7)	0.001
Vasopressor treatment, n (%)	39 (40)	34 (35)	5 (5)	< 0.001

Table 2. *Antecedents, reason of ICU admission and etiologies*

	All patient (n = 97)	non-AKI (n = 37)	AKI Stage 1 (n =47)	AKI Stage 2 (n =12)	AKI Stage 3 (n =1)	AKI all (n =60)	p-AKI vs. non-AKI
Antecedents							
Smoking, n (%)	16 (16)	8 (22)	5 (11)	3 (25)	0 (0)	8 (13)	0.285
High blood pressure n (%)	22 (22)	7 (19)	13 (28)	1 (8)	1 (100)	15 (25)	0.487
Diabetes, n (%)	30 (31)	9 (24)	16 (34)	4 (33)	1 (100)	21 (35)	0.269
Heart Disease n (%)	28 (29)	5 (13)	18 (38)	5 (42)	0 (0)	23 (38)	0.009
Malignancy, n (%)	4 (4)	2 (5)	1 (2)	1 (8)	0 (0)	2 (3)	0.635
Reason of ICU admission							
Disturbances of consciousness, n (%)	69 (71)	25 (67)	35(74)	9 (75)	0 (0)	44 (73)	0.543
Shock, n (%)	19 (20)	1 (3)	12 (253)	6 (50)	0 (0)	18 (30)	0.001
Respiratory distress, n (%)	47 (48)	17 (46)	25 (53)	4 (33)	1 (100)	30 (50)	0.698
One distress, n (%)	70 (72)	32 (86)	29 (62)	8 (67)	1 (100)	38 (63)	0.013
Two distresses, n (%)	17 (17)	5 (13)	11 (23)	1 (8)	0 (0)	12 (20)	0.414
Three distresses, n (%)	10 (10)	0 (0)	7 (15)	3 (25)	0 (0)	10 (17)	0.012
Etiologies							
Septic Shock, n (%)	29 (30)	1 (3)	22 (47)	6 (50)	0 (0)	28 (47)	<0.001
Hypovolemic Shock,n (%)	29 (30)	1 (3)	22 (47)	6 (50)	0 (0)	28 (47)	<0.001
Cardiogenic shock, n (%)	17 (17)	1 (3)	14 (30)	2 (17)	0 (0)	16 (27)	0.003
Severe sepsis, n (%)	71 (73)	20 (54)	40 (85)	10 (83)	1 (100)	51 (85)	0.001
HHS, n (%)	15 (15)	2 (5)	7 (15)	6 (50)	0 (0)	13 (22)	0.031
DIN, n (%)	10 (10)	5 (13)	4 (8)	1 (8)	0 (0)	5 (8)	0.498

AKI : acute kidney injury HHS : hyperosmolar hyperglycemic state DIN : drug-induced nephrotoxicity Case numbers and percentage ratios, according to the appropriate groups.

Table 3. *Mortality and length of stay*

Parameters	All patients (n =97)	non-AKI (n =37)	Acute Kidney Injury				p-AKI all vs. non-AKI
			Stage 1 (n =47)	Stage 2 (n =12)	Stage 3 (n =1)	AKI all (n =60)	
Length of stay in hospital before ICU admission (days), median (IQR)	1[1-2]	1[1-1]	1[1-2]	1[1-3]	1[1-1]	1[1-2]	0.097
ICU stay (days), median (IQR)	4[1-7]	3[1-7]	4[1-7]	3[1-8]	5[5-5]	4[1-7]	0.778
ICU mortality, n (%)	35(36)	4(11)	25(53)	6(50)	0(0)	31(52)	<0.001

Table 4. *Logistic regression analysis of the variables (SAPS II 30, Shock,* heart disease*) focused on AKI all.*

Variables	OR	IC at 95%	p
Heart disease	6	2-21	0.005
Shock	27	3-228	0.002
SAPS II 30	6	2 -21	0.005

4. Discussion

AKI is a common complication of critical illness.[12] The increased incidence of AKI is most likely due to a trend of admitting older, more severely and more chronically ill patients to hospitals.[10,13-16] We found an incidence of AKI equal to 62%. Different studies describe a wide range of AKI (5.2%-67.2%), which varies across ICUs and admission diagnoses.[14, 17-25] There are few studies which assessed the prevalence according to the AKI stages. [5,14,19] and have found it between 22%-35.5%, with different degrees of severity: AKI 1: 17.5%-19.1%, AKI 2: 2.4%- 3.8% and AKI 3: 2%-12.5%.[5, 26]

In our study, AKI patients were significantly older with

significantly higher severity scores. In the aging population, there is heightened susceptibility to drug toxicity, partially owing to altered drug pharmacokinetics and pharmacodynamics. Furthermore, elderly people consume twice medications including nephrotoxic agents, than younger patients.[16,27] Sepsis, hypovolemia, nephrotoxic drugs and cardiovascular diseases are among the common causes of AKI in elderly patients.[28]

The sepsis and septic shock represent the most frequent causes of morbidity and mortality in the ICU.[1] The multicentre European Sepsis Occurrence in Acutely Ill Patients (SOAP) study found that 51% of septic patients developed AKI.[29] More recently, in a 1-day point prevalence survey for severe sepsis/septic shock from 454 ICUs in Germany, concomitant AKI was reported in 41.4% of septic patients.[30] Likewise, two large multicentre observational studies of critically ill patients with AKI found sepsis to be a contributing factor in 46% to 48% of episodes of AKI.[4, 30] In our study, sepsis was also the leading etiologic factor (in 85% of patients) of AKI.

Patients with Acute decompensate heart failure are commonly accompanied by comorbidities such as hypertension, diabetes mellitus, and atherosclerosis which are the risk factors for kidney disease.[31] Acute worsening of renal function in acute decompensate heart failure might be a consequence of new onset kidney injury or acute deterioration of preexisted chronic kidney disease.[31] More than 70% of patients hospitalized for acute decompensate heart failure will experience acute worsening of renal function, which is associated with significantly poor outcomes.[31]

Cardiogenic shock associated renal hypoperfusion is strongly associated with AKI.[5] In our study 27 % of AKI was related to cardiogenic shock. The incidence of acute cardio-renal syndrome in patients with AKI is estimated to be between 19% and 45%.[32] In a large cohort study of patient after cardiac arrest, it was found that AKI occurs in nearly 50% of patients. [33] This indicates that the severity of hypoxia/ischemia may also have an effect on the development of AKI. Marenzi *et al* (2010) found that in the setting of ST-elevation acute myocardial infarction, complicated by cardiogenic shock, AKI occurred in 55% of patients.[34]

We noted that all patients presenting hypovolemia have also a septic shock (47%). Medve *et al* (2011) found that 39% of AKI was related to hypovolemia.[5] We do not determine specific diagnostic criteria to classify prerenal conditions, because of the lack of standardized definitions and the difficulty in assessing reversibility of AKI, the concept of prerenal failure has been recently challenged.[5,35]

In our study the proportion of patients who had HHS, during their ICU stay presented significantly more AKI than others (p=0.031). People with diabetes may be at increased risk of developing AKI.[36] AKI may occur as a result of the severe fluid depletion associated with diabetic ketoacidosis and non-ketotic HHS.[36] The presence of underlying diabetic nephropathy may predispose to AKI resulting from adverse effects such as hypotension, sepsis or exposure to nephrotoxic agents.[36] The increased incidence of cardiovascular disease may also lead to renal impairment as a result of complications of ischemic heart disease or renal artery atherosclerosis.[36]

Rhabdomyolysis commonly occurred in patients with HHS, induces AKI and this could aggravate their clinical course and increase mortality.[37,38]

In our study, 5 patients (8 %) presented AKI potentially drug-related. However, the kidneys are vulnerable to injury due to their high filtration capacity and high metabolic activity, and most drugs, especially hydrophilic drugs and their metabolites, are eliminated largely by kidneys in urine, thus increasing the risk of DIN.[39] DIN accounts for 18 - 27% of community- and hospital-acquired episodes of AKI.[39] Future research should focus on identification and validation of novel predictive biomarkers of kidney injury and development of DIN-specific classification and staging system.[39,40]

In our study, the proportion of patients who needed mechanical ventilation and vasopressor during their ICU stay differ significantly in patients with AKI vs patients without AKI. This result is similar to those reported.[5, 41] We could not distinguish that the mechanical ventilation or the vasopressor treatment was a cause or a consequent of AKI.

Mortality was significantly more frequent in patients with AKI than in patients without AKI. It is known, that primary renal failure, secondary to a variety of pathologic conditions affecting the kidney has relatively good outcome and low mortality (5-10%).[41-44] Pre-renal factors like dehydration or hypotension, which can be easily corrected, result in rapid renal recovery.[1] In contrast, the onset of AKI, as a part of multiple organ failure has 50-70% mortality.[8,18] In addition, patients who survive AKI have a higher rate of long-term mortality, and other adverse outcomes than patients who survive hospitalization without AKI.[45] At AKI diagnosis, routine clinical data may be helpful for predicting adverse outcomes.[12] The higher mortality of AKI in our patients can be explained also by factors, such as higher incidence of non-uniform treatment principles, patients often present late for treatment leading to increased complications and the high incidence of nosocomial sepsis.

AKI wasn't increased significantly the median length of stay at the ICU. These results are different than those reported by others studies.[1, 5, 41]

Shock, history for heart disease and a SAPSII score >30 were independent risk factors for development of AKI these finding are similar to other studies.[5, 30-34]

We noted that the proportion of patients presenting AKI and treated by renal replacement therapy was very low comparing to other studies.[5] Perhaps because of our low effective of patients with stage 3. But we believe that acute renal replacement therapy should be more developed in our regional hospital.

5. Limits of Study

Our study protocol did not require an invasive hemodynamic monitoring; we could not assess exactly the volume-status of patients on ICU-admission. We evaluated it as a major limitation of our study because the diagnosis of hypovolemia was based mainly on basic hemodynamic data and clinical impressions. Finally, we didn't distinguish early and late AKI. As some patients developed AKI before admission to the ICU, others within the first 24 hours of admission to the ICU, others more would have developed delayed AKI several days after admission to the ICU. The moment of occurrence of AKI during ICU stay could affect patient outcome.

Moreover, we are unable to assess long-term outcome or renal recovery.

6. Conclusion

We have a prospective, epidemiological study on AKI, occurring at representative. The results of the present study confirm that AKI has a high incidence and a high mortality in medical intensive care patients. Shock, history for heart disease and a SAPSII score >30 were independent risk factors for development of AKI. Future prospective studies are needed to better understand the reasons for those results and define opportunities for further improvement in patient outcomes as in many cases AKI is preventable and treatable.

Abbreviations

AKI: acute kidney injury; ICU: intensive care unit; SAPS II: simplified acute physiology score; HHS :Hyperosmolar hyperglycemic state ; DIN : drug-induced nephrotoxicity;

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