



Acute kidney injury in critically ill patients with COVID-19: prevalence, risk factors and mortality in eastern Morocco

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Abstract

Introduction Acute kidney injury (AKI) is commonly seen in critically ill hospitalized patients with COVID-19 and its incidence reaches 60% in this setting. The aim of this work was to determine the prevalence, characteristics, risk factors and mortality of AKI in patients admitted to the intensive care unit (ICU) for COVID-19.

Patients and methods This observational retrospective case series was conducted between February 1, 2020 and December 31, 2020 at the ICU of the university hospital Mohammed VI of Oujda, Morocco. All COVID-19 patients hospitalized in the ICU with acute respiratory failure were included. AKI was defined and classified into three stages using the KDIGO criteria 2012. We excluded patients with end-stage kidney disease and those who were under 18 years old.

Results Six hundred adult patients were included and 65.5% of them were men. Sixty patients had minimal lung damage (< 25%), 105 patients had mild lung damage (25–50%), 186 had severe lung damage (50–75%) and 193 patients had very severe lung damage (> 75%). A total of 210 patients (35%) developed AKI, of whom 78 (37.2%) had mild AKI (stage 1) and 132 (62.8%) severe AKI (stages 2 and 3). Patients in the severe and mild AKI groups had a higher rate of comorbidities, especially hypertension (mild AKI [46.2%] vs. severe AKI [36.4%] vs. no AKI [27.4%], $p = 0.002$) and diabetes (mild AKI [52.6%] vs. severe AKI [33.3%] vs. no AKI [26.4%], $p < 0.001$). During hospitalization, 23.3% of patients with AKI received kidney replacement therapy. In-hospital mortality was observed in 51.3% for mild AKI, 55.3% for severe AKI and 21% in patients who did not have AKI ($p < 0.001$).

Conclusion Our findings revealed that not only severe AKI, but also mild AKI was correlated to in-hospital mortality. Whatever the severity of the kidney impairment, it remains a major prognostic element.

Keywords Acute kidney injury · Covid-19 · Risk factors · Mortality · Morocco

Introduction

Acute respiratory distress syndrome is the most severe but uncommon expression of the Coronavirus disease-19 (COVID-19), leading to hospitalization in an intensive care unit (ICU). In this context of severe forms, acute kidney injury (AKI) is relatively common and increases the global risk of morbidity and mortality. The incidence of AKI in patients with COVID-19 is between 3 and 6%, rising to 15–58% in those patients who are critically ill [1, 2]. This incidence also varies depending on the definition of AKI in the study, criteria for admission to ICU, and criteria for hospitalization. Indeed, the type of serum creatinine measurement technique may also be a contributing factor, especially for slight variations in low creatinine values. Mortality exceeds 50% in stage 3 AKI and increases with the initiation of kidney replacement therapy [3, 4]. The pathophysiology

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of this AKI is multifactorial and is mainly linked to fluid balance disorders, toxic tubular damage following cytokine release syndrome or rhabdomyolysis, angiotensin II pathway activation, a complex process driven by virus-mediated injury, thrombotic events and intravascular coagulation, organ crosstalk and drug nephrotoxicity. The aim of this work was to determine the prevalence, characteristics, risk factors, prognosis and mortality of AKI in patients admitted to the ICU for COVID-19.

Patients and methods

Design of the study: This observational case series was conducted between February 1, 2020, and December 31, 2020, at the ICU of the university hospital Mohammed VI of Oujda. We included COVID-19 adult patients hospitalized in the ICU with acute respiratory failure requiring high-flow nasal oxygen therapy, non-invasive or mechanical ventilation, while we excluded patients with disease regardless of whether they were on dialysis or not, patients under the age of 18, and patients who died within 48 h of admission. COVID-19 was confirmed by a positive reverse-transcriptase polymerase chain reaction test of nasopharyngeal swab specimens or by meeting clinical and epidemiological criteria with typical chest imaging. AKI was defined and classified into three stages using the Kidney Disease Improving Global Outcomes (KDIGO) criteria 2012, based on serum creatinine and diuresis [5]. Mild AKI was defined as stage 1, and severe AKI was defined as stage 2 or stage 3. All creatinine measurements were performed using a standardized Jaffe kinetic technique within the same laboratory. Statistical Analyses: The Mann–Whitney *U* test was used for continuous variables and the χ^2 test or Fisher's exact test for categorical variables as appropriate. The risk factors associated with AKI were identified by multivariate analysis in binary logistic regression. The study was performed following the ethical standards laid down in the Declarations of Helsinki and Istanbul. The need for written, informed consent was waived due to the retrospective and observational nature of this research.

Results

From February 1, 2020, to December 31, 2020, 614 adult patients were admitted to the ICU with acute respiratory failure caused by COVID-19 infection, of whom 600 were included in this study. Of the 14 excluded patients, 11 had ESRD, and 3 were under 18 years old. The median age of included patients ($n = 600$) was 65 (58–77) years, and 403 (67.2%) were men. Sixty patients (11%) had minimal damage (estimated at less than 25% of the lung tissue),

105 patients (19.3%) had mild lung damage (estimated at 25–50% of the lung tissue), 186 (34.2%) had severe lung damage (estimated at 50–75% of the lung tissue, and 193 patients (35.5%) had critical lung damage (estimated at > 75% of the lung tissue). All patients were isolated and received the basic treatment using azithromycin, vitamin C, zinc, vitamin D and corticosteroids. Eighty-one patients (13.5%) with high levels of interleukin 6 received intravenous Tocilizumab (400 mg). Noninvasive ventilation and mechanical ventilation were required in 23.3% and 32.5% of cases, respectively. A total of 210 patients (35%) developed AKI, of whom 78 (37.2%) had mild AKI (stage 1), and 132 (62.8%) had severe AKI (stages 2 and 3). Table 1 reports the main data (clinical, comorbidities, laboratory, radiological, therapeutics, outcomes and complications) in the different groups of patients: mild AKI, severe AKI and without AKI. In multivariate analysis, independent factors associated with AKI (mild and severe) were as follows: advanced age (OR 1.02, 95% confidence interval CI 1.00–1.04, $p = 0.02$), diabetes (OR 2.83, CI 1.62–4.95, $p < 0.001$), history of chronic kidney disease (OR 25.89, CI 6.81–98.41, $p < 0.001$), diarrhea (OR 2.58, CI 1.28–5.18, $p = 0.008$), septic shock (OR 4.34, CI 2.24–8.43, $p < 0.001$), need for mechanical ventilation (OR 2.23, CI 1.21–4.10, $p = 0.01$), disseminated intravascular coagulation (OR 5.0, CI 2.05–12.20, $p < 0.001$), ferritin blood level (OR 1.0, CI 1.00–1.00 $p = 0.001$) and procalcitonin blood level (OR 1.03, CI 1.00–1.06, $p = 0.02$).

In-hospital mortality was 53.8% in patients who had AKI (51.3% for mild and 55.3% for severe AKI) compared to 21% in patients who did not have AKI ($p < 0.001$). The median time to death was 14.7 [20, 25.3], 10.2 [13, 15.7], and 11.1 [13, 14.9] days in the group without AKI, the group with mild AKI and the group with severe AKI, respectively ($p = 0.001$). Severe complications such as ischemic complication, pulmonary embolism and septic shock were higher in the AKI group, particularly in the severe AKI group, also explaining the high mortality rate of both AKI groups.

Discussion

Of the 600 patients admitted to our ICU for severe COVID-19, one third (35%) developed AKI. Among the 210 patients who developed AKI, 23.3% required dialysis, and 53.8% died. The global incidence of AKI assessed using the KDIGO definition ranged from 10 to 80% in previously published series [3, 6]. In a large population of COVID-19 patients hospitalized in metropolitan New York, Hirsch et al., reported that the prevalence of comorbidities such as hypertension, diabetes, and cardiovascular disease, and the need for invasive mechanical ventilation and vasopressor drugs were all independently associated with AKI, which is consistent with our study [7]. The biological markers of

Table 1 Clinical characteristics, comorbidities, laboratory data, therapeutics, outcomes and complications in severe COVID-19 patients admitted to the Intensive Care Unit

| Parameters N=600 | Patients without AKI N=390 | Patients with mild AKI N=78 | Patients with severe AKI N=132 | p value |
|---|-------------------------------|--------------------------------|-----------------------------------|---------|
| <i>Clinical data and comorbidities, n (%)</i> | | | | |
| Age, years (median quartiles) | 63 (50–72) | 71 (60–81) | 64 (55–71) | <0.001 |
| Male patients | 256 (65.5) | 50 (64.1) | 97 (73.5) | 0.209 |
| Arterial hypertension | 107 (27.4) | 36 (46.2) | 48 (36.4) | 0.002 |
| Diabetes | 103 (26.4) | 41 (52.6) | 44 (33.3) | <0.001 |
| Smoking | 25 (6.4) | 4 (5.1) | 14 (10.6) | 0.205 |
| Asthma | 20 (5.1) | 0 | 2 (1.5) | 0.029 |
| Other pulmonary diseases | 6 (1.5) | 0 | 1 (0.8) | 0.454 |
| Heart disease | 34 (8.7) | 23 (29.5) | 22 (16.7) | <0.001 |
| Neoplasm | 10 (2.6) | 2 (2.6) | 5 (3.8) | 0.756 |
| Stroke | 5 (1.3) | 3 (3.8) | 1 (0.8) | 0.172 |
| <i>Laboratory data, median (IQR)</i> | | | | |
| Leukocyte count, 10 ³ /L | 9.48 (6.74–13.4) | 11.6 (9.3–16.4) | 11.8 (8.30–16.01) | <0.001 |
| Lymphocyte count, 10 ³ /L | 0.91 (0.58–4.70) | 0.78 (0.55–1.195) | 0.73 (0.45–1.16) | 0.002 |
| Platelet count, 10 ³ /L | 242 (178.5–320) | 217 (160–316) | 234 (148–299) | 0.158 |
| D-dimers, mg/L | 1.10 (0.38–3.70) | 1.5 (0.61–4.42) | 2.60 (0.69–7.90) | 0.003 |
| C-reactive protein, mg/l | 159 (67–230) | 209 (144–288) | 202 (87–270) | <0.001 |
| Procalcitonin, ng/mL | 0.24 (0.13–0.64) | 0.73 (0.32–4.03) | 0.91 (0.30–4.20) | <0.001 |
| Lactose dehydrogenase, UI/L | 554 (354–764) | 592 (422–862) | 598 (403–918) | 0.015 |
| Serum creatinine, mg/l | 7.9 (6.70–10.02) | 14 (10.03–18.84) | 14.10 (8.00–48.84) | <0.001 |
| Serum ferritin, µg/L | 801 (371–1619) | 843 (371–2061) | 1372 (608–2767) | <0.001 |
| <i>Therapeutic data, n (%)</i> | | | | |
| Intermittent hemodialysis | 0 (0) | 0 (0) | 29 (21.5) | <0.001 |
| Continuous venovenous filtration | 0 (0) | 0 (0) | 20 (15.2) | <0.001 |
| High nasal flow oxygen | 196 (50.3) | 45 (57.7) | 70 (53) | 0.464 |
| Continuous positive airway pressure | 39 (10) | 6 (7.7) | 27 (20.5) | 0.003 |
| Non-invasive ventilation | 97 (24.9) | 15 (19.2) | 28 (21.2) | 0.453 |
| Mechanical ventilation | 80 (20.6) | 37 (47.4) | 78 (59.1) | <0.001 |
| Extracorporeal membrane oxygenation | 7(1.1) | 0 | 18 (3) | 0.002 |
| <i>Outcomes, n (%)</i> | | | | |
| Ischemic stroke | 4 (1) | 3 (3.8) | 0 (0) | 0.039 |
| Ischemic complications | 54 (13.8) | 19 (24.4) | 38 (28.8) | <0.001 |
| Pulmonary embolism | 24 (6.2) | 4 (5.1) | 10 (7.6) | 0.757 |
| Disseminated intravascular coagulation | 12 (3.1) | 8 (10.3) | 27 (20.5) | <0.001 |
| Septic shock | 45 (11.6) | 28 (35.9) | 70 (53) | <0.001 |
| In-hospital mortality | 82 (21) | 40 (51.3) | 73 (55.3) | <0.001 |

inflammation and organ failure were more marked in the AKI group in our study. The same result has been observed in numerous published studies [3, 6].

In three large published series, the use of dialysis was reported in 11.1% (Nimkar et al., US), 19% (Chan et al., US), and 14.3% (Hirsch, US), among COVID-19 patients with AKI, respectively [2, 3, 7]. In our study, 23.3% of all patients with AKI required dialysis. This relatively high frequency of dialysis need can be explained by the fact that all the patients included in our study were admitted to the

ICU and all were in critical condition. In the series reported by Nimkar et al., mortality was observed in 58.1% of the patients in the AKI group vs. 19.6% in the group without AKI ($p < 0.001$) [2]. Chan et al. reported mortality in 50% in the AKI group vs. 8% in the group without AKI ($p < 0.001$) [3], while in the series of Hirsch et al. mortality was 35% in stage 1 AKI group vs. 90% in stage 3 AKI, and 50% in the AKI group requiring dialysis [11]. Overall, mortality rate was higher in the severe forms of AKI, in particular in stage 3 according to the KDIGO classification and in the forms of

AKI requiring dialysis [2, 3, 7]. In the series of Gupta et al., AKI requiring dialysis in COVID-19 patients was observed in 46% and AKI was identified as a risk factor for mortality [8]. In the Spanish series of Pineiro et al., involving severe AKI in critically ill COVID-19 patients, AKI requiring dialysis was observed in 28.8% of cases and mortality was reported in 1.9% of AKI stage 2 KDIGO vs. 38.5% of AKI stage 3 KDIGO [9]. The risk factors associated with AKI that were identified in multivariate analysis testify to the severity of the clinical and biological parameters, particularly in the presence of comorbidities such as diabetes.

In summary, our study, performed in eastern Morocco, shows that also in our setting AKI stage 2 and 3 according to the KDIGO classification, is associated with a high mortality rate that exceeds 50% in patients admitted to the ICU.

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Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical statement The study was performed following the ethical standards laid down in the Declarations of Helsinki and Istanbul.

Informed consent The need for written, informed consent was waived due to the retrospective and observational nature of this research.

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