Acute kidney injury in critically ill obstetric patients: a cross-sectional study in an intensive care unit in Northeast Brazil

Lesão renal aguda em pacientes obstétricas gravemente doentes: um estudo transversal em uma unidade de terapia intensiva do nordeste do Brasil

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Abstract

Introduction: Acute kidney injury (AKI) is a complication still poorly studied in the setting of obstetric patients, which is associated with increased mortality. Objective: The aim of this study was to investigate the frequency and risk factors of AKI among critically ill obstetric patients. **Methods:** A cross-sectional study was conducted with all patients admitted to an intensive care unit (ICU) due to obstetric complications, in Fortaleza, Brazil, in the period between January 2012 and December 2014. AKI was defined according to AKIN criteria. **Results:** A total of 389 patients were included, aged between 13 and 45 years. The main causes of ICU admission were pregnancy-related hypertensive syndromes (54.5%), hemorrhage and hemorrhagic shock (12.3%), heart diseases (9.0%), respiratory insufficiency (8.2%) and sepsis (5.4%). AKI was found in 92 cases (24%), and this was the most frequent complication. General mortality was 7.5%, and mortality due to AKI was 21% (p = 0.0007). In the multivariate analysis, risk factors for AKI were cesarian delivery (95% CI = 0.23-0.85, p = 0.01) and thrombocythopenia (95% CI = 1.50-4.36, p = 0.001). AKI was an independent risk factor for death (OR = 6.64, 95% CI = 3.11-14.15, p < 0.001). **Conclusion:** AKI was the main complication among critically ill obstetric patients and it was associated with increased mortality. Most cases were associated with pregnancy-related hypertensive disorders, which are complications that can be easily identified and treated during prenatal care.

Keywords: intensive care units; mortality; pregnancy; renal insufficiency.

Resumo

Introdução: A lesão renal aguda (LRA) é uma complicação ainda pouco estudada no contexto das pacientes obstétricas, que está associada com aumento da mortalidade. **Objetivo:** Investigar a frequência e os fatores de risco da LRA entre pacientes obstétricas. Métodos: Foi realizado estudo transversal com todas as pacientes admitidas em uma unidade de terapia intensiva (UTI) devido a complicações obstétricas em Fortaleza, Brasil, no período de janeiro de 2012 a dezembro de 2014. LRA foi definida de acordo com o critério AKIN. **Resultados:** Foram incluídas 389 pacientes, com idade entre 13 e 45 anos. As principais causas de admissão na UTI foram síndromes hipertensivas da gestação (54,5%), hemorragia e choque hemorrágico (12,3%), cardiopatias (9,0%), insuficiência respiratória (8,2%) e sepse (5,4%). LRA foi encontrada em 92 casos (24%), e esta foi a complicação mais frequente. A mortalidade geral foi de 7,5%, e a mortalidade por LRA foi de 21% (p = 0,0007). Na análise multivariada, os fatores de risco para LRA foram parto cesariano (IC 95% = 0,23-0,85, p = 0,01) e plaquetopenia (IC 95% = 1,50-4,36, p = 0,001). LRA foi um fator de risco independente para óbito (OR = 6,64, IC 95% = 3,11-14,15, p < 0,001). **Conclusão:** LRA foi a complicação mais frequente em pacientes obstétricas gravemente doentes e esteve associada com aumento da mortalidade. A maioria dos casos esteve associada às síndromes hipertensivas da gravidez, que são complicações passíveis de tratamento durante o pré-natal.

Palavras-chave: gravidez; Insuficiência renal; mortalidade; unidades de terapia intensiva.

Introduction

Acute kidney injury (AKI) is a frequent complication among hospitalized patients, which affects around 5% of patients in clinical wards and 10-30% of those in intensive care units (ICU).[1] Among obstetric patients AKI is not frequent and is still poor studied.[2,3] The main conditions associated with AKI in the gestational-puerperal period are: pre-eclampsia, eclampsia, post-partum hemorrhage, HELLP syndrome, puerperal sepsis and intravascular disseminated coagulation, and in severe cases it can also require dialysis.[4] In a previous smaller study in our region, among 55 obstetric patients with AKI requiring dialysis, the main causes of AKI were: pregnancy-associated hypertension, including HELLP syndrome (41.8%), puerperal sepsis (14.5%), placenta previa (9.1%), hemolytic uremic syndrome (9.1%) and thrombotic thrombocytopenic purpura (5.5%).[2]

In the last 50 years, there as a significant decrease in the incidence of obstetrics-associated AKI, but it is still a current public health problem in developing countries, once AKI is associated with increased mortality, and death is not an expected event to occur during the gestational-puerperal period.[5]

The aim of this study was to investigate the frequency and risk factors of AKI among critically ill obstetric patients.

Methods

This is a cross-sectional study conducted with all patients with obstetric complications admitted to the intensive care unit (ICU) of the Maternidade-Escola Assis Chateaubriand, in Fortaleza, Northeast of Brazil, in the period from January 2012 to December 2014. This ICU is a reference Obstetric service in the region, and the protocol of the study was reviewed and approved by the Ethics Committee of the institution (protocol nº 875.394/2014).

Inclusion criteria were: patients admitted due to obstetric complications during the study period. Medical records were reviewed and information regarding patients' age, cause of ICU admission, type of delivery, clinical manifestations and complications during ICU stay and outcome were retrieved.

A comparison between patients with and without AKI was performed, and risk factors for AKI were investigated. AKI was defined according to the "Acute Kidney Injury Network" (AKIN) criteria.[6]

Results were expressed by mean ± standard deviation or frequencies. The statistical analysis consisted of univariate and multivariate analysis of clinical and laboratory data, which was performed using the SPSS 20.0 software. Comparison of the parameters for the two groups (AKI *versus* non-AKI) was done using Student's *t* test and Fisher's exact test. Analysis of correlations between AKI and categorized risk factors employed Fisher's exact test, Pearson's chi-squared test and the verisimilitude ratio test.

A logistic regression model was used for quantitative variables. Adjusted odds ratios and 95% confidence intervals were calculated. Multivariate logistic regression was performed to analyze the possible risk factors for AKI. The factors included in the multivariate model were those that showed a significance level < 20% in the univariate analysis (Mann-Whitney test and chi-squared test). Descriptive values below 5% (p value < 0.05) were considered statistically significant.

Results

A total of 389 patients were included, and AKI was found in 92 cases (24%). Patients' mean age was 27.1 ± 7.1 years (range 13-45), and the most affected age group was 35-45 years. The main causes of ICU admission were: pregnancy-related hypertensive syndromes (54.5%), hemorrhage and hemorrhagic shock (12.3%), heart diseases (9.0%), respiratory insufficiency (8.2%), sepsis (5.4%) and others less frequent comorbidities (10.6%).

The comparison of clinical and laboratory data between patients with and without AKI is shown in Tables 1 and 2. The main comorbidities associated with AKI were: HIV (66.6%), pyelonephritis (60%), liver disease (60%), coagulation disturbances (54.5%), *diabetes mellitus* (38.4%) and chronic hypertension (30.9%). Use of vasoactive drugs and antibiotics was seen in 40.2% and 29% of cases, respectively. Among all complications seen during ICU stay, AKI was the most frequent (24%), followed by hypotension (15.5%), hemorrhage (10.2%) and sepsis (6.7%).

In the multivariate analysis, factors associated with AKI were: cesarian delivery (OR=0.45, 95% CI = 0.23-0.85, p = 0.01) and thrombocytopenia (OR = 2.56, 95% CI = 1.50-4.36, p = 0.001).

A total of 28 deaths were observed (7.5%), and the main causes were: sepsis/multiple organ failure (32%), encephalic death (25%) and hemorrhagic

Table 1 Comparison of clinical characteristics of obstetric patients admitted to an intensive care unit according to the occurrence of acute kidney injury

	AKI (n = 92)	Non-AKI (n = 297)	*p*
Age (years)	27.1 ± 7.1	25.6 ± 7.3	0.08
Prenatal care	55 (59.7%)	185 (62.2%)	0.90
Type of delivery**	19 (20.6%)	30 (10.1%)	0.01
Vaginal	69 (75%)	234 (78.7%)	
Cesarian			
Hypertension	13 (14%)	29 (9.7)	0.25
Diabetes mellitus	5 (5.4%)	8 (2.6%)	0.19
Lenght of ICU stay (days)	6.6 ± 5.9	6.8 ± 15.4	0.92
Time on mechanical ventilation (days)	2.7 ± 4.8	2.7 ± 12.4	0.99
$SBP_{admission}$ (mmHg)	127 ± 33	126 ± 27	0.73
$DBP_{admission}$ (mmHg)	80.3 ± 25.9	80.5 ± 20.9	0.96
Complications during ICU stay			
Respiratory insufficiency	5 (5.4%)	18 (6.0%)	1.0
Liver disease	6 (6.5%)	4 (1.3%)	0.01
Coagulation disturbances	6 (6.5%)	5 (1.6%)	0.02
Sepsis	8 (8.6%)	20 (6.7%)	0.49
Hypotension	24 (26%)	38 (12.7%)	0.005
Hemorrhage	18 (19.5%)	22 (7.4%)	0.002
Metabolic acidosis	59 (64%)	115 (38%)	0.001
Thrombocytopenia	48 (52%)	75 (25%)	< 0.001
Leukocitosis	71 (77%)	202 (68%)	0.13
Anemia	35 (38%)	90 (30%)	0.20
Treatment			
Use of vasoactive drugs	29 (31.5%)	43 (14.4%)	0.001
Use of antibiotics	52 (56.5%)	127 (42.7%)	0.02
Use of diuretics	62 (67.3%)	148 (49.8%)	0.004
Mechanical ventilation	38 (41.3%)	76 (25.5%)	0.006

*ICU = intensive care unit; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; Student *t*, Fisher and chi-square tests. Significant $p < 0.05$. **Missing delivery data is referent to pre-delivery death or missing information on medical records.

shock (21%); 19 of these deaths were among patients with AKI (20.6%). AKI was an independent risk factor for death (OR = 6.64, 95% CI = 3.11-14.15, $p < 0.001$).

Discussion

The present study investigated the occurrence of AKI among patients admitted to an ICU due to obstetrics complications in a single reference unit from Brazil. A high incidence of AKI was observed and it was associated with high mortality (> 20%). AKI is one of the main conditions associated with poor prognosis in the ICU setting. Obstetric causes of AKI are not common in developed countries, but are still an important public health problem in the developing world which reflects the precarious prenatal care.

AKI in critically ill patients has a prevalence varying from 20 to 30%, and dialysis is required in around 60% of cases.[7,8] In pregnancy, AKI is still not well studied, and its determinant factors should be better investigated. It is estimated that AKI occur in 1 out of 10,000-20,000 pregnancies in developed countries.[8,9]

In the present study, the main causes of admission were pregnancy-associated hypertensive syndromes (more than half of cases), which is in accordance with previous studies showing that these are the main complications of pregnancy. The main causes of AKI in obstetric patients are hypertensive disorders,

Table 2 Comparison of laboratory data of obstetric patients admitted to an intensive care unit according to the occurrence of acute kidney injury

	AKI (n = 92)	Non-AKI (n = 297)	*p*
Urea (mg/dL)$_{admission}$	49.2 ± 24.2	24.2 ± 13.6	< 0.001
Creatinine (mg/dL)$_{admission}$	1.6 ± 0.9	0.6 ± 0.1	< 0.001
Creatinine (mg/dL)$_{maximum}$	1.9 ± 1.0	0.6 ± 0.1	< 0.001
Creatinine (mg/dL)$_{discharge}$	1.4 ± 0.9	0.5 ± 0.1	< 0.001
pH$_{admission}$	7.2 ± 0.1	7.3 ± 0.08	< 0.001
HCO$_{3\ admission}$	16.3 ± 5.3	20.0 ± 3.8	< 0.001
Hematocrit (%)$_{admission}$	31.1 ± 8.3	32.4 ± 6.7	0.15
Hemoglobin (g/dL)$_{admission}$	10.4 ± 2.6	10.9 ± 2.2	0.12
Leukocytes (x3/mm^3)$_{admission}$	19147 ± 9583	16317 ± 7434	0.04
Platelets (x3/mm^3)$_{admission}$	159621 ± 103416	215569 ± 105030	< 0.001
AST (UI/L)$_{admission}$	380 ± 880	96 ± 268	< 0.001
ALT (UI/L)$_{admission}$	177 ± 469	53 ± 123	< 0.001

*Student *t* test. Significant $p < 0.05$.

hemorrhage and sepsis,[2,10-18] as also observed in our study. Most of these complications can be prevented with adequate prenatal care.

AKI was the main complication observed in this study. In general ICUs, AKI occur in around 20-40%,[19] so the incidence of AKI in our study is in accordance with the literature. In a previous study in our region, AKI occurred in less than 1% of cases, but only severe AKI was considered (AKI requiring dialysis).[2] Among the comorbidities found in our study, HIV was the most frequent (66% of AKI cases). It is known that HIV contributes to increase maternal mortality,[15] mainly in African countries,[20] because it favors infections and sepsis development, which represents the main causes of maternal mortality around the world.[21]

There was a higher frequency of cesarian delivery among patients with AKI in the present study. It is possible that such delivery was indicated due to pregnancy complications, such as pre-eclampsia and eclampsia. It can also be associated with hemorrhagic complications, as suggested by previous studies, in which AKI in the obstetric setting was associated with hemorrhage in 31.4% of cases.[22]

Length of hospital stay and time in mechanical ventilation was similar in both groups (AKI *versus* non-AKI). Blood pressure levels at admission were also similar in both groups, but AKI was associated with hemorrhage and hypotension. Regarding laboratory tests, liver enzymes were higher among AKI patients and platelets levels were lower, which is in accordance with a previous study that linked these findings to a higher incidence of AKI.[23] These laboratory abnormalities are probably associated with liver disorders, coagulation disturbances and HELLP syndrome.[2,8,24-27]

Regarding treatment, the use of vasoactive drugs, antibiotics, diuretics and mechanical ventilation were more frequent among AKI patients, which reflect the clinical severity of these patients. Mechanical ventilation and use of vasoactive drugs are associated with maternal mortality according to previous studies.[18]

Mortality rates in obstetric-related AKI can be as high as 30%,[2] and measures to prevent it must be implemented. In the present study, mortality among AKI patients was 20.6%, significantly higher than in those without this complication. Bouaziz *et al.*[26] have also found a higher mortality among critically ill patients with AKI in comparison with those without AKI (9.3% *vs.* 1.7%, $p < 0.001$).

In summary, AKI was the most frequent complication of obstetric patients admitted to the ICU and an important risk factor for death. Most cases were associated with pregnancy-related hypertensive disorders, which are complications that can be easily identified and treated during prenatal care.

Study limitations

Main limitations of this study derive from its retrospective nature. Some data from patient's records were not available on admission. Urine output and urinalysis were particularly poorly available and it was not

frequently accurately measured, so it was not included in our analysis. We know that pregnancy involves the mother and the baby, so it would be important to have information on fetal/neonatal outcomes, but it was not possible to include in this study due to lack of information in the medical records that were consulted.

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