Severity and hospitalization time of non-critical patients with Acute Kidney Injury

Gravidade e tempo de hospitalização de pacientes não críticos com lesão renal aguda

Gravedad y tiempo de internación de pacientes no críticos con Lesión Renal Aguda

ABSTRACT

Objective: To assess severity and hospitalization time of non-critical patients with Acute Kidney Injury (AKI). **Methods:** A prospective and observational study conducted with 137 patients, with data collected by means of a structured questionnaire. The chi-square, Fisher's exact and Mann-Whitney tests were used for statistical analysis and results were considered significant with p≤0.05. The research was approved by the Research Ethics Committee. **Results:** Oxygen therapy by macro-nebulization resulted in higher mortality both during hospitalization (*p*=0.001) and after discharge (*p*=0.02), as well as in high sodium levels (*p*=0.0001 vs. *p*=0.005) and occurrence of kidney injury or failure (*p*=0.02 vs. *p*=0.02). The need for ventilatory support increased the hospitalization time by 3.02 times (*p*=0.02). **Conclusion:** Acute Kidney Injury was frequent in more than half of the patients, with KDIGO 2 and 3 severity levels, which were associated with in-hospital and post-discharge mortality. The most severe patients (KDIGO 3) remained hospitalized for longer periods of time. Macro-nebulization in patients with tracheostomy tripled the hospitalization time.

Descriptors: Hospitalization; Nursing; Acute Kidney Injury; Mortality.

RESUMO

Objetivo: avaliar gravidade e tempo de hospitalização de pacientes não críticos com lesão renal aguda. **Métodos:** estudo observacional prospectivo com 137 pacientes realizado por meio de questionário estruturado para coleta de dados. Os testes qui-quadrado, exato de Fisher e Mann-Whitney foram empregados para análise estatística e considerou-se significativo resultado com *p*≤0,05. Aprovado pelo Comitê de Ética em Pesquisa. **Resultados:** oxigenoterapia por macronebulização resultou em maior mortalidade durante internação (*p*=0,001) e após alta hospitalar (*p*=0,02), assim como níveis elevados de sódio (*p*=0,0001 vs. *p*=0,005) e a ocorrência de lesão ou falência renal (*p*=0,02 vs. *p*=0,02). Necessidade de suporte ventilatório aumentou em 3,02 vezes o tempo de hospitalização (*p*=0,02). **Conclusão:** A lesão renal aguda foi frequente em mais da metade dos pacientes, sendo KDIGO 2 e 3 níveis de gravidade que se associaram com mortalidade intra-hospitalar e pós-alta. Paciente de maior gravidade (KDIGO 3) permaneceu maior tempo hospitalizado. A macronebulização em pacientes com traqueostomia triplicou o tempo de internação.

Descritores: Hospitalização; Enfermagem; Lesão Renal Aguda; Mortalidade.

RESUMEN

Objetivo: evaluar la gravedad y el tiempo de internación de pacientes no críticos con Lesión Renal Aguda. **Métodos:** estudio observacional y prospectivo realizado con 137 pacientes en el que se utilizó un cuestionario estructurado para recopilar los datos. Para el análisis estadístico se utilizaron las pruebas Chi-cuadrado, Exacta de Fisher y Mann-Whitney, y se consideraron significativos resultados con *p*≤0,05. El estudio fue aprobado por el Comité de Ética en Investigación. **Resultados:** con la oxigenoterapia con macronebulización se presentó mayor mortalidad durante la internación (*p*=0,001) y después del alta hospitalaria (*p*=0,02), así como niveles elevados de sodio (*p*=0,0001 vs. *p*=0,005) e incidencia de daño o insuficiencia renal (*p*=0,02 vs. *p*=0,02). La necesidad de soporte ventilatorio aumentó 3,02 veces el tiempo de internación (*p*=0,02). **Conclusión:** La Lesión Renal Aguda fue frecuente en más de la mitad de los pacientes, con niveles de severidad KDIGO 2 y 3 que se asociaron con mortalidad intrahospitalaria y después del alta. Los pacientes más graves (KDIGO 3) permanecieron internados por más tiempo. La macronebulización en pacientes con traqueostomía triplicó el tiempo de internación.

Descriptores: Internación; Enfermería; Lesión Renal Aguda; Mortalidad.

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INTRODUCTION

Population aging and the increased prevalence of hypertension and diabetes *mellitus* have exerted impacts on the growth in the number of hospitalizations due to Acute Kidney Injury (AKI)[1], a condition characterized by sudden loss of renal function over hours or days, resulting in inability to maintain the electrolyte, acid-alkaline and water balances.

There have been advances in the definition of AKI and in the opportunities for prevention and support measures, but mortality remains high[2] and, despite improvements in the prevention opportunities, even mild AKI is associated with an increased risk of death[3].

Failures in AKI early recognition and in active monitoring of the renal function lead to the development of end-stage kidney disease[4]. Consequently, better understanding the severity of AKI and of its impacts on hospitalization time represents a potential indicator of the efficiency of preventive measures[4].

Diverse evidence highlights that AKI and its progression can be prevented in some circumstances, mitigating its consequences with timely and effective care measures[5-6]. However, care strategies for patients with AKI are not totally defined[7], which reinforces the importance of better understanding this syndrome in different scenarios, such as the one of non-critical patients.

Undoubtedly, hospitalized patients need a detailed evaluation. Therefore, intensity, frequency and duration of monitoring should be individualized according to the characteristics of the patient and of the resources[7].

In hospitalization units, monitoring of the renal function is usually less detailed and less frequent, with hardly intensive checks of vital signs and incomplete measurement of urinary volume, which can delay the identification of elevated serum creatinine and, consequently, of renal damage. Given this context, the objective of this study was to assess the severity and hospitalization time of non-critical patients with AKI.

METHOD

A quantitative, prospective, observational and longitudinal study developed at the Medical Clinic of a large-size public hospital in the Brazilian Midwest region between 2018 and 2019. The sample was non probabilistic and for convenience, consisting of 137 patients selected according to serum creatinine change confirmed in laboratory tests. The sample losses during the patients' monitoring were due to the absence of biochemical markers to evaluate renal function and death.

Sample calculation was based on the comparison of quantitative variables from two groups, with a 5% significance level, average size effect (d=0.4) and a beta value of 90%. The patients included were those aged at least 18 years old, hospitalized in the Medical Clinic, and with creatinine change according to the Kidney Disease Improving Global Outcomes (KDIGO 1, 2 or 3)[8]. The patients subjected to tests with contrast and to Palliative Care were excluded.

The patients were diagnosed with AKI when presenting an increase equal to or higher than 0.3 mg/dL in the baseline serum creatinine value for at least 48 hours and after admission to the Medical Clinic, as well as reduced estimated glomerular filtration (eGFR) rates for seven days, according to KDIGO[8]. Baseline creatinine was the lowest value in the first week of hospitalization in the Medical Clinic[9], considering that most of the patients did not have their creatinine levels recorded in their medical records for the 365 days prior to hospitalization.

AKI severity was assessed by means of the serum creatinine criterion from the KDIGO classification, as follows: KDIGO 1 (mild severity), characterized by an 1.5-to-1.9-fold increase in baseline creatinine; KDIGO 2 (intermediate severity) represented by a 2-to-2.9 fold increase in baseline creatinine; and KDIGO 3 (high severity), characterized by a 3-fold increase in baseline creatinine, by a 4.0 mg/dL increase, or by initiation of dialysis therapy[8].

For data collection, a structured questionnaire created by the researchers was elaborated and the following data were extracted from the patients' medical records on a weekly basis: sociodemographic variables (age, gender, skin color), mobility status (bedridden, able to walk), level of consciousness (conscious, lethargic, comatose, confused), clinical variables (Body Mass Index, comorbidities), biochemical markers (serum creatinine, sodium, potassium and hemoglobin), hemodynamic status (mean blood pressure and axillary temperature), hospitalization time, death and discharge.

Monitoring of the patients' laboratory tests was performed for six months after AKI identification, whether they remained hospitalized or not, which made it possible to identify their clinical profile and outcome. From hospital discharge, telephone contacts were made with the patients to warn them about the need to maintain control of the biochemical markers (serum creatinine and urea) at 30, 60, 90 and 180 days. The tests had the date predefined and collection was supported by the Primary Health Care support network. After 30 days, the outcome (death during hospitalization of after discharge) was verified in the medical record.

The clinical evaluation of hemodynamic and laboratory parameters followed the institutional protocol set forth by the *Distrito Federal* State Health Department, linked to the Brazilian Unified Health System: mean blood pressure (MBP) change when ≤60 mmHg or ≥100 mmHg, temperature from 35.8°C to 37°C, serum sodium from 135 mEq/L to 148 mEq/L, serum potassium from 3.6 mEq/L to 5 mEq/L, serum creatinine from 0.7 mg/dL to 1.2 mg/dL, and serum hemoglobin from 13 g/dL to 17 g/dL[10]. Charlson's Comorbidity Index (CCI) was calculated to assess the patients' overall severity considering the sum of the weights from 0 to 6 attributed to 17 clinical conditions[11]. CCI is an easy-to-apply method to assess patients' severity and takes into account the comorbidities to estimate the mortality risk[11].

The results were expressed as centrality (mean, median) and dispersion (25th and 75th quartiles and standard deviation) measures. The Statistical Package for the Social Sciences (SPSS), version 23, was used for the statistical analysis. The association between variables was analyzed using the Chi-square (likelihood ratio), Fisher's and Mann-Whitney tests, as appropriate, and Odds Ratios (ORs) and their respective 95% Confidence Intervals (95% CIs) were calculated. p-values≤0.05-were considered significant.

The study was submitted and approved by the Research Ethics Committee, according to Resolution 466/2012 of the National Health Council, under Certificate of Presentation for Ethical Appreciation (*Certificado de Apresentação de Apreciação Ética*, CAAE) 51576215.8.0000.5553, and all patients signed the informed consent form.

RESULTS

A total of 137 patients were monitored in the Medical Clinic, most of them male (73; 53.3%) and with preserved level of consciousness (96; 70.1%); their mean age was 64±15 years old and they presented a mean Body Mass Index (BMI) of 26.4±7.4 kg/m². The most frequent skin color was black (32.8%) and more than half of the patients were bedridden while in the Medical Clinic (56.2%).

Arterial hypertension (96; 70.1%), diabetes *mellitus* (67; 48.9%), respiratory diseases (49; 35.8%) and heart diseases (47; 34,3%) were the most incident comorbidities. The most frequent outcome was hospital discharge (88; 64.2%), although 19.7% and 20.4% of the patients evolved to death during their hospitalization in the Medical Clinic and after hospital discharge, respectively. The median hospitalization time corresponded to 34 (18-58) days.

AKI was confirmed in 75 (54.7%) patients, based on persistent creatinine and eGFR change

for at least seven days during hospitalization, with 19.7% presenting intermediate severity (KDIGO 2). The least severe (KDIGO 1) and most severe (KDIGO 3) AKI conditions affected 17.5% of the patients.

Patients with higher sodium levels, using a tracheostomy cannula and who died during hospitalization or after discharge from the Medical Clinic ward evolved to more severe AKI (KDIGO 2 or 3) (Table 1).

Table 1 – Correlation of the clinical variables with occurrence or non-occurrence of KDIGO 1, 2 or 3 AKI among patients hospitalized in a non-critical care unit. *Distrito Federal* (DF).

Characteristics		No dysfunction or KDIGO 1 (n=86)	KDIGO 2 or 3 (n=51)	*p*-value
Age (years old)	Med (25-75)	66 (49-78)	67 (57-77)	0.8
Male gender	n (%)	48 (55.8%)	25 (49.0%)	0.4
BMI (kg/m^2)	Med (25-75)	25.1 (21.1-28.2)	25.0 (22.5-29.2)	0.5
ATB use	n (%)	20 (23.3%)	9 (17.6%)	0.4
Number of ATBs	Med (25-75)	2 (1-3)	2 (2-3)	0.9
CCI>3		42 (49.4%)	21 (41.2%)	0.4
CCI	Med (25-75)	3 (2-5)	3 (2-4)	0.6
TCT use (macro-nebulization)	n (%)	74 (86.0%)	29 (56.9%)	<0.0001
Hemoglobin (g/dL)	Med (25-75)	11.0 (9.6-13.3)	10.2 (9.4-12.6)	0.3
Potassium (mEq/L)	Med (25-75)	4.3 (3.9-4.7)	4.2 (3.6-4.8)	0.5
Sodium (mEq/L)	Med (25-75)	137 (134-141)	142 (136-150)	<0.0001
Death during hospitalization in the MC	n (%)	10 (11.8%)	17 (34.0%)	0.002
Death after discharge from the MC	n (%)	29 (34.9%)	28 (56.0%)	0.02
Hospitalization time in the MC (days)	Med (25-75)	35 (18-54)	34 (19-63)	0.4

BMI – Body Mass Index; ATB – Antibiotic; CCI – Charlson's Comorbidity Index; TCT – Tracheostomy ; MC – Medical Clinic; Chi-square test (likelihood ratio); Fisher's Exact Test; Mann-Whitney test. Source: The authors.

Less severe patients (no AKI or KDIGO 1) were administered a thiazide diuretic (*p*=0.04) and also required macro-nebulization as ventilatory support (*p*<0.0001). Higher serum sodium levels was a clinical condition found in the patients with their renal function most severely affected (KDIGO 2 and 3) (*p*<0.0001).

Mortality was significant among older patients, both during the hospitalization period (*p*<0.001) and after hospital discharge (*p*=0.003). Charlson's scores above 3 were significantly more related to the patients' death after hospital discharge.

Using tracheostomy with macro-nebulization resulted in higher mortality in both groups, during

hospitalization (*p*=0.001) and after hospital discharge (*p*=0.02), as well as in higher sodium levels (*p*=0.0001 *vs.* *p*=0.005) and in kidney injury (KDIGO 2) or failure (KDIGO 3) (*p*=0.02 *vs.* *p*=0.02). However, mortality predominated especially after hospital discharge in the patients with greater severity as diagnosed by CCI>3 (*p*=0.007) and who presented reduced hemoglobin levels (*p*=0.03).

Number of antibiotics (*p*=0.02) and reduced hemoglobin levels (*p*=0.007) contributed significantly to longer hospitalization times, and need for macro-nebulization in patients with tracheostomy increased the hospitalization time by 3.02 times (*p*=0.02) (Table 2).

Table 2 – Association between hospitalization time and clinical variables. *Distrito Federal* (DF).

Variables	Hospitalization time ≤21 days (n=40)	Hospitalization time >21 days (n=93)	Odds Ratio	95% Confidence Interval	p
Demographic variables					
Age (years old)	66 (47-78)	67 (55-77)	1.0	0.98-1.03	0.90
Male gender	22 (55.0%)	48 (51.6%)	0.87	0.41-1.83	0.70
BMI (kg/m²)	25.3 (20.6-31.1)	25.0 (22.4-27.9)	0.98	0.94-1.03	0.80
White skin color	5 (33.3%)	10 (23.3%)	0.61	0.17-2.19	0.50
ATB					
ATB use	31 (77.5%)	75 (80.6%)	1.21	0.49-2.98	0.20
Number of ATBs	2 (1-3)	2 (2-3)	1.58	1.07-2.33	0.02
CCI					
CCI>3	15 (37.5%)	45 (48.9%)	1.60	0.75-3.41	0.20
CCI	3 (2-4)	3 (2-5)	1.12	0.92-1.38	0.30
Oxygen therapy					
O$_2$ mask	2 (5.0%)	12 (12.9%)	2.82	0.60-13.21	0.20
TCT use (macro-nebulization)	5 (12.5%)	28 (30.1%)	3.02	1.07-8.50	0.02
Laboratory variables					
Hemoglobin (g/dL)	11.6 (10.0-12.3)	10.5 (9.0-12.3)	0.79	0.67-0.93	0.007
Potassium (mEq/L)	4.4 (3.9-4.8)	4.3 (3.8-4.7)	0.90	0.53-1.53	0.70
Sodium (mEq/L)	137 (135-145)	139 (135-145)	1.01	0.98-1.05	0.50
Pathologies					
AKI	22 (55.0%)	51 (54.8%)	0.99	0.47-2.09	0.90
KDIGO 2 and 3	13 (32.5%)	37 (39.8%)	1.37	0.63-3.00	0.40

ATB – Antibiotic; Charlson's Comorbidity Index; TCT – Tracheostomy; AKI – Acute Kidney Injury; Chi-square test (likelihood ratio); Fisher's Exact test; Mann-Whitney test.

Source: The authors.

DISCUSSION

The findings show that more than a half of the patients evolved to AKI and that prolonged hospitalization times were more frequently associated with more severe conditions (CCI>3; 48.9%), which in the analysis grounds significant in-hospital and post-discharge mortality.

Despite advances in the definition of this pathology, in prevention strategies and in support measures, AKI of different severity degrees (KDIGO 1, 2 and 3) proved to be a frequent condition, and mortality of the patients with greater renal impairments (KDIGO 2 or 3) was 34% during the hospitalization period and 56% after discharge. This evidences that, even after hospital discharge, i.e., for those who survived hospital discharge, the prognosis proves to be unfavorable. In fact, event mild AKI (KDIGO 1) is associated with a 50% increased risk of death[4].

Aged patients, predominantly male and overweight, frequently evolve to AKI, a common severe complication during hospitalizations that generally leads to prolonged hospitalization times[4]. These clinical characteristics were also observed in 67.88% of the patients in the current study, especially when the hospitalization period exceeded 21 days.

AKI is characterized as a syndrome that carries along a high burden, especially in developing countries, considering the possibility of AKI progression to end-stage disease and the insufficiency of treatment resources, conditions that reveal the importance of early recognition and active monitoring of the renal function[4,12].

In addition to that, age ($p<0.001$ vs. $p=0.003$), macro-nebulization ($p=0.001$ vs. $p=0.02$), hypernatremia ($p<0.0001$ vs. $p=0.005$), kidney injury (KDIGO 2) or failure (KDIGO 3) ($p=0.02$ vs. $p=0.02$) showed an association with in-hospital and post-discharge mortality, and need for macro-nebulization due to tracheostomy was a factor that led to a three-fold increase in hospitalization time. CCI values above 3 ($p=0.007$) and low hemoglobin levels ($p=0.03$) were associated with post-discharge mortality, which evidences disease severity and the need for continuous monitoring of the patients. A clinical trial revealed that persistent AKI (lasting more than seven days), called Acute Kidney Disease[13], can be associated with worse clinical outcomes, including longer hospitalization times[14]. On the other hand, some of the factors associated with mortality are preventable and, therefore, patients may benefit from early identification and treatment measures, at least regarding the reversible conditions[4].

It is noted that reduced hemoglobin can be a functional marker for kidney disease severity, increasing the risk for recurrent AKI[15] and, consequently, hospitalization times, which was also significantly revealed in this study ($p=0.007$), as was the case with mortality during the post-discharge period ($p=0.03$).

In addition to that, comorbidities such as diabetes and arterial hypertension may increase the risk of AKI, and these chronic conditions were also frequently identified in our study. Acknowledged as a public health problem, AKI imposes the need to adopt strategies for early detection and preventive measures[15].

Morbidity and death, common conditions in patients with AKI in the intensive care scenario[16], were also frequent in this research, although the study explored the non-critical scenario, which reinforces the need for good practices such as those described in the clinical guidelines of the KDIGO classification[8], such as monitoring of at-risk patients.

Early identification of factors associated with AKI, such as high serum sodium levels and dependence on oxygen therapy, observed in the current research, may reduce the number of readmissions and complications[17]. Hospitalized patients may present certain unbalance between oxygen supply and demand, with predisposition to hypoxemia and renal oxidative stress, determinants of changes in homeostasis[16] and potential AKI inducers, for example. In milder cases (KDIGO 1), the kidney is able to self-regulate and still preserves the glomerular filtration rate and glomerular filtration pressure; however, these mechanisms fail in the more advanced stages of renal damage (KDIGO 2 and 3)[18], leading to progressive deterioration of the renal function[16] and to higher mortality rates[19].

Patients classified as KDIGO 2 or 3 evolved to more severe forms, with need for oxygen support – tracheostomy ($p<0.0001$), change in the sodium levels ($p<0.0001$), and death both during hospitalization ($p=0.002$) and after discharge from the Medical Clinic ($p=0.02$).

In this context, the findings of this study reinforce the need to develop methods to improve AKI prevention, such as training programs based on guidelines, referral to a nephrologist, and surveillance by means of an electronic data system[20]. It is also important to value the role of the multidisciplinary team, especially the Nursing team, in performing careful clinical monitoring, hydroelectrolyte control, and hypovolemia and hypotension corrections[17].

The deaths during hospitalization and after hospital discharge totaled 40.1% and were associated with more severe AKI (KDIGO 2 and 3; $p=0.02$). In line with the findings of the current study, a cohort study developed in Scotland[21] and another one conducted in Spain[22] show a relationship between renal impairment severity and death. Although scientific advances can

be noticed, AKI and its complications require new interventions due to the complexity of the clinical condition[23] and to the absence of specific and sensitive biomarkers for early detection in the clinical practice[24], which increases the risks and, thus, the need to devise care guides to reduce worse prognoses and avoid the development of chronicity patterns[25].

In this context, monitoring may favor the implementation of preventive strategies combined with educational measures and electronic alerts such as care bundles more easily integrated in the non-critical scenario[17].

The limitations of this study include its single-center approach, the impossibility of measuring urinary volume, its small sample size and the measuring bias risk. However, its findings contribute to scientific knowledge because they describe factors related to disease severity and hospitalization time in non-critical patients, in addition to favoring the systematization of individualized and qualified care.

CONCLUSION

Acute Kidney Injury was frequent in more than half of the patients, with KDIGO 2 and 3 severity levels that were associated with in-hospital and post-discharge mortality. The most severe patients (KDIGO 3), according to CCI, remained hospitalized for longer periods of time. Macro-nebulization in patients with a tracheostomy tripled the hospitalization times.

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