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Original Research Article

Incidence of Community- Acquired Versus intensive care unit Acquired Acute Kidney Injury in Two Tertiary intensive care units among aged patients

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Abstract

Acute Kidney Injury is increasing over the last years despite advances in health care system. Elderly had higher chances of experiencing acute kidney injury with devastating effects. A prospective study was conducted on elderly aged ≥ 60 years who were admitted to two intensive care units, over 6 months. Acute kidney injury was diagnosed based on Kidney Disease: Improving Global Outcomes criteria, 2012. All patients admitted to any of the two intensive care units with acute kidney injury, community acquired acute kidney injury (CA.AKI) or developed acute kidney injury during the stay, intensive care unit acquired AKI (ICUA.AKI), were identified. The study included 196 critically ill elderly patients. Their mean age was 68.2± 5.5. The incidence of Acute Kidney Injury "AKI" was 22.4%, 16.3% had CA.AKI and 6.1% had ICUA.AKI. Patients with AKI had significantly higher age and baseline renal failure on dialysis and higher prevalence of risk factors including septic shock, hypovolemia and anemia. Regarding outcomes, patients with AKI had significantly worse SOFA, and more discharge with new acute kidney disease "AKD". In ICUA.AKI, septic shock, diuretic use and higher age were the significant predictors for the occurrence of AKI. In CA.AKI, hypovolemia, older age and lower hemoglobin were the significant predictors for the occurrence of AKI.

Keywords: Acute kidney injury, Critically ill, Elderly, Predictors, Septic shock.

INTRODUCTION

Acute kidney injury (AKI), previously termed acute renal failure (ARF), has attracted more attention in recent years as a result of its rising incidence and its devastating effect on patients (Chertow et al., 2005).

The cultural, economic and geographical differences determine the epidemiology of AKI in different places. Therefore, the epidemiology of AKI differs from country to country and also varies from center to center within the same country (Cerda et al., 2005; Kaufman et al., 1991).

Yearly, AKI affects 0.3-0.5% of community dwelling patients, 5-10% of all hospitalized patients, 25-70% of intensive care unit (ICU) patients (Chertow et al., 2005; De Mendonça et al., 2000; Hsu Cy et al.,2007) with 3 fold higher risk for hospital mortality and prolonged hospital length of stay (Chertow et al., 2005; Ali et al., 2007).

Aging is associated with a decline in organ function and the emergence of chronic diseases as a result of the

accumulated damages to these vulnerable organ systems (Liu et al., 2012).

The incidence of AKI is increasing despite advances in health care and may be related to the aggressive increase in medical and surgical therapies in elderly patients with multiple comorbidities (Coca, 2010), in addition to the more exposure to common risk factors for AKI (Cerda et al., 2008).

Furthermore, some patients develop AKI prior to hospitalization; community acquired AKI (CA.AKI).

Many studies confirmed that the incidence of CA.AKI was 2 to 3 times higher than hospital acquired AKI (HA.AKI) (Der Mesropian et al., 2014), however both had the same prognosis regarding the higher length of stay, mortality and overall health care costs (Chertow et al., 2005; Der Mesropian et al., 2014).

Scanty researches are available about CA.AKI versus HA.AKI in moderate income countries, especially in the critically ill aged group.

This prospective study described risk factors, epidemiology and short term outcomes of AKI in elderly, and compare between CA.AKI and intensive care unit acquired AKI (ICUA.AKI), in two tertiary general hospitals ICU centers.

MATERIALS AND METHODS

Study Design

A prospective study was conducted on all elderly subjects aged ≥ 60 years who were admitted to either of the general ICU El-Sahel Hospital or the geriatric ICU Ain Shams University Hospital, during the study period from August 2015 to February 2016.

Using Epi info program, the required sample size is 68 persons to detect AKI in ICU, using data not restricted to elderly (Chertowet al., 2005; De Mendonça et al., 2000; Hsu Cy et al., 2007).

Data collection

Patients were subjected to complete blood picture, blood urea nitrogen, creatinine, electrolytes, and arterial blood gas analysis. Past medical history was reported from old medical reports and their proxy relatives.

The study had been approved by the ethical committees of El-Sahel Hospital and Geriatrics and Gerontology department, Ain Shams University Hospital. Informed consent was obtained from all next kin.

AKI was diagnosed based on Kidney Disease: Improving Global Outcomes criteria (KDIGO, 2012). Any patients admitted to any of the two ICUs with AKI (CA.AKI) or developed AKI during the ICU stay (ICUA.AKI) were identified.

Sequential Organ Failure Assessment (SOFA) scoring system was used to describe organ functions from laboratory data to get severity score. The scores were calculated from 0-4 points for each organ (cardiovascular, respiratory, hepatic, renal, neurological and coagulation organs) according to the dysfunction level and then the scores of all systems were summed to give the final score (Vincent et al., 1996).

Statistical data analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 16 (SPSS Inc., Chicago, IL, USA).

Qualitative data were presented in the form of frequency tables. Quantitative data were presented in the form of means and SD or median (interquartile) values (Zhang, 2016). Normality distribution of the variables was tested using one sample Kolmogorov-Smirnov test. For quantitative data, differences between two groups were assessed using the Student's t-test or Mann-Whitney U test. For qualitative data, the Chi-square test or Fisher's Exact test was used to compare between the two groups.

Binary regression analysis was used to determine the most significant predictors of CA.AKI and ICUA.AKI.

RESULTS

In this prospective study, from August 2015 to February 2016, 196 critically ill elderly patients were admitted to the two ICUs under study. Their mean age was 68.2±5.5. The incidence of AKI was 22.4%, 16.3% had CA.AKI and 6.1% had ICUA.AKI

Patients with AKI had significantly higher age (P value <0.001) and baseline renal failure (RF) on dialysis and higher prevalence of risk factors including septic shock, hypovolemia and anemia (P value= 0.002, 0.004 and < 0.001consecutively).

Regarding outcomes, patients with AKI had significantly worse SOFA, and more discharge with acute kidney disease "AKD" (Table 1).

No history of radio-contrast induced AKI among the patients and aminoglycosides were used by a single patient.

Patients with ICUA.AKI had higher age and higher prevalence of hypovolemia, septic shock and diuretic use than those with CA.AKI. Patients with ICUA.AKI had worse SOFA score than those with CA.AKI (Table 2).

Older age, hypovolemia and anemia were significant predictors of CA.AKI, while older age, septic shock and diuretic use were significant predictors of ICUA.AKI (Table 3).

Table 1. Descriptive statistics of patients with and without AKI

Variables	**Patients with AKI** N=44	**Patients without** AKI N= 152	P value
Age	71.32± 3.6	67.3± 5.7	<0.001
Male	22 (50%)	80 (52.6%)	0.45
Baseline comorbidities:			
DM	16 (36.4%)	73 (48%)	0.17
HTN	20 (45.5%)	76 (50%)	0.59
Congestive heart failure	4 (9.1%)	13 (8.6%)	0.91
Ischemic heart disease	11 (25%)	45 (29.6%)	0.55
Baseline renal failure on dialysis	3 (6.8%)	0 (0%)	0.011[#]
Risk factors:			
Infection	24 (54.5%)	71 (46.7%)	0.23
Sepsis	23 (52.3%)	66 (43.4%)	0.38
Septic shock	11 (25%)	12 (7.9%)	0.002
Hypovolemia	20 (45.5%)	35 (23%)	0.004
Anemia	35 (79.5%)	69 (45.4%)	<0.001
Diuretics	8 (18.2%)	15 (9.9%)	0.13
Laboratory data:			
Hemoglobin	9.9± 2.3	12.1± 2.7	<0.001
Sequel:			
Blood transfusion	15 (34.1%)	21 (13.8%)	0.002
SOFA score	7 (5-11)	3 (2-5)	<0.001
Death	24 (54.5%)	61 (40.1%)	0.13
Discharge with AKD	9 (20%)	0 (0%)	0.001

[#]Fisher's Exact test

Qualitative data were expressed in the form of number (frequency). Quantitative data were expressed in the form of mean ± SD, or median (interquartiles).

AKD: acute kidney disease, AKI: Acute Kidney Injury, CA.AKI: Community Acquired Acute Kidney Injury, DM: Diabetes Mellitus, HTN: Hypertension, ICUA.AKI: Intensive Care Unit Acquired Acute Kidney Injury, SOFA: Sequential Organ Failure Assessment.

Table 2. Descriptive statistics of patients with CA.AKI and ICUA.AKI:

Variables	**Patients with CA.AKI**, N= 32	**Patients with ICUA.AKI,** N= 12	P value
Age	70.7± 3.8	72.9± 2.4	0.029
Male	17 (53.1%)	5 (41.7%)	0.49
Baseline comorbidities:			
DM	11(34.4%)	5 (41.7%)	0.46[#]
HTN	16 (50%)	4 (33.3%)	0.26[#]
Congestive heart failure	2 (6.2%)	2 (16.7%)	0.28
Ischemic heart disease	7 (21.9%)	4 (33.3%)	0.73[#]
Baseline renal failure on dialysis	2 (6.2%)	1 (8.3%)	1[#]
Risk factors:			
Infection	15 (46.9%)	9 (75%)	0.09
Sepsis	14 (43.8%)	9 (75%)	0.07
Septic shock	4 (12.5%)	7 (58.3%)	0.004
Hypovolemia	11 (34.4%)	9 (75%)	0.016
Anemia	26 (81.2%)	9 (75%)	0.65
Diuretics	3 (9.4%)	5 (41.7%)	0.013
Laboratory data:			
Hemoglobin	9.9± 2.3	9.89± 2.3	0.96
Highest serum creatinine	4.15± 2.5	3.64± 1.6	0.78
Δ in serum cretinine	0.3 (0- 0.3)	0.4 (0- 0.75)	0.37
AKI severity:			
Stage I AKI	27 (84.4%)	9 (75%)	
Stage II AKI	1 (3.1%)	1 (8.3%)	0.7

Table 2. Continue

Stage III AKI	4 (12.5%)	2 (16.7%)	
Sequel:			
Blood transfusion	10 (31.2%)	5 (41.7%)	0.52
SOFA score	6.5 (4-9)	11 (7- 13.75)	0.04
Death	15 (46.9%)	9 (75%)	0.09
Discharge with AKD	9 (28.1%)	0 (0%)	0.14

[#]Fisher's Exact test
Qualitative data were expressed in the form of number (frequency). Quantitative data were expressed in the form of mean ± SD, or median (interquartiles).
AKD: acute kidney disease, AKI: Acute Kidney Injury, CA.AKI: Community Acquired Acute Kidney Injury, DM: Diabetes Mellitus, HTN: Hypertension, ICUA.AKI: Intensive Care Unit Acquired Acute Kidney Injury, SOFA: Sequential Organ Failure Assessment.

Table 3. Predictors of AKI occurrence

Predictors of CA.AKI[#]					
Variables	Beta	SE	95% CI	OR	P value
Hypovolemia	2.47	0.53	(4.2-33.4)	11.87	<0.001
Age	0.13	0.045	(0.6-0.9)	1.13	0.005
Hemoglobin	-0.26	0.096	(0.6-0.9)	.77	0.007
Predictors of ICUA.AKI[#]					
Variables	Beta	SE	95% CI	OR	P value
Septic shock	3.34	1.04	(3.7- 219)	28.34	0.001
Diuretics	2.73	1.09	(1.8- 121)	15.34	0.012
Age	0.25	0.08	(1.1- 1.49)	1.28	0.001

[#]The following variables were considered in the initial model: septic shock, hypovolemia, diuretics, age and hemoglobin
AKI: Acute Kidney Injury, CA.AKI: Community acquired Acute Kidney Injury, ICUA.AKI: Intensive Care Unit Acquired Acute Kidney Injury.

DISCUSSION

The current search compared CA.AKI and ICUA.AKI, in two tertiary general hospitals ICU centers, among elderly subjects aged ≥ 60 years. A study by Feest et al. (Feest et al., 1993) found that patients older than 60 yr of age have a three to eight-fold, age-dependent increase in the frequency of CA.AKI.

The scanty data about AKI in elderly, in developing countries, could be attributed to the predominance of elderly AKI in developed rather than developing countries where it is a disease of young (Kohli et al., 2007). Therefore, there are difficulties in defining the incidence of AKI especially when a subject searches for data about elderly in developing countries, the place of residence of ≥ 50% of the world's population (Cerda et al., 2008).

Few literatures concerned with community acquired versus ICUA.AKI, therefore most of the discussion compared the results with literatures discussing CA.AKI versus HA.AKI, not restricted to the elderly because of its scanty data.

In the current geriatric group, ICU patients, the incidence of AKI were higher than Wonnacott et al. and Xu et al. (Wonnacott et al., 2014; Xu et al., 2015) who studied AKI in hospitals, their results were 6.4% and 11.6% consecutively versus 22.4%, in the current study.

The Wonnacott et al. (Wonnacott et al., 2014) study, in two district general hospitals, included low socioeconomic participants in a representative sample, and Xu et al. (Xu et al., 2015) study was conducted among Chinese patients. However, the lower incidence in both studies could be attributed to the inclusion of all admissions to the both centers, not only elderly.

The incidence of ICUA.AKI in the current group was lower than the incidence of HA.AKI in China in the very elderly group (≥80years old), 6.1% versus 14.8% (Wen et al., 2013).This may be explained by the lower mean age of the current study. By 80 years old, glomerular filtration rate and effective plasma flow reach half that of youth (Silva, 2005).

In agreement with the current ICUA.AKI, Uchino et al. (Uchino et al., 2005) reported an AKI incidence in 5.7% of patients, from multi-centers with age range of 53-75 years who were admitted to an ICU.

The incidence of CA.AKI was higher than studies in the general population, not restricted to the elderly (Wonnacottet al., 2014; Aitken et al., 2013).

This agreed with a study done by Ghita et al. (Ghita et al., 2015) in Morocoo on 210 patients having AKI, aged 57.2±19.2 which revealed that CA.AKI was more common than HA.AKI reaching 74.8% of the patients with a diagnosis of AKI versus 72% in the current study.

Recent subanalysis of Ge et al. (Ge et al., 2016) study was published in 2016 discussing elderly AKI in Chinese patients, aged ≥ 65 years old. Patients with CA.AKI were lower than current results, 10.47% versus 16.3%, while the prevalence of HA.AKI was much higher 27.19%, even in those aged 65–79 years, it were 11.55% versus 6.1%.

This variation could be attributed to the significant role of hypovolemia as a predictor of CA.AKI which seems to be less significant in their study due to the nature of the current study as ICU based one. On the other hand, the higher prevalence in their HA.AKI might reflect changes in patients' management between the two different socioeconomic cultures as more radio-contrast induced AKI was noted in the Chinese study 16% versus 0% in the present study.

In the current results, patients with AKI were older than those without AKI. Anemia followed by hypovolemia then septic shock and baseline RF on dialysis were the predominant risk factors in patients with AKI, which were significantly higher in the AKI group.

The most common risk factors for ICUA.AKI were infection, sepsis, hypovolemia, anemia, septic shock and diuretic use, and from comorbidities ischemic heart disease and hypertension which is in agreements with other results; (Wen et al., 2013), in HA.AKI among very elderly, where infection, hypovolemia, drugs then cardiovascular diseases were the predominant risk factors.

Furthermore, Han et al. (Han et al., 2015) reported the higher risk for AKI in anemic patients with odd ratio 2.43. Higher age, hypovolemia, septic shock and diuretic use were significantly higher in ICUA.AKI than CA.AKI as risk factors, with no significant difference in baseline comorbidities, including diabetes mellitus, hypertension, ischemic heart disease and congestive heart failure, which is in agreement with previous literatures (Wonnacott et al., 2014; Ghita et al., 2015; Bagshaw et al., 2009).

In ICUA.AKI, septic shock, diuretic use and higher age were the significant predictors for the occurrence of AKI, as confirmed in a study by Levi et al.(Levi et al.,2012) which was done on 134 Brazilian elderly patients admitted to ICU with average age 64 years.

The use of nephrotoxic drugs is unavoidable and there is controversy about them, their use with the adequate adjustment is the available way, with low agreement among the sources, (Medscape®, DRUGDEX®, UpToDate® and the Brazilian Therapeutic Formulary), for drug-induced nephrotoxicity (Bicalho et al., 2015). On the contrary, because oliguria is a risk factor for AKI, many clinicians use high doses of furosemide to increase urine output, and its beneficial effect is not established (van der Voort et al.,2009).The deleterious effect of furosemide is supported by the current findings, although the diuretic group did not have more oliguria, hypovolemia or septic shock. This might be attributed to direct nephrotoxic effect of the furosemide which needs to be further elicited in other researches.

In CA.AKI, hypovolemia, age and hemoglobin were the significant predictors for the occurrence of AKI.

It was approved by 2 studies done by Kufman et al. (Kufman et al., 1991) and Ghita et al. (Ghita et al., 2015) who found that hypovolemia due to decreased fluid intake, vomiting, diarrhea, diuretics or bleeding was the most significant contributing cause for CA-AKI. As older patients were more exposed to dehydration especially if they are bedridden or demented dependent on others with poor access to fluids, in addition the age related physiological changes causing impairment of their thirst sensation.

Some researchers found that patients with CA.AKI were more presented with severe AKI, with better survival, therefore they could not have a clear explanation (Wonnacott et al., 2014) while others found no difference in AKI severity between CA.AKI and hospital acquired AKI as the current results (Ghita et al., 2015; Chien-Ning et al., 2016).

Regarding outcomes, patients with AKI had worse SOFA score than those without AKI and discharged more significantly with AKD. In addition, patients with ICUA.AKI had worse SOFA score than those with CA.AKI.

Previous literatures Cerda et al.(Cerda et al., 2008) and Bucaloiu et al. (Bucaloiu et al., 2012) have found increased risks of de novo CKD following AKI with incomplete recovery.

In the current study, there was increased mortality in patients with AKI (54.5%) in comparing with elderly patients with no AKI, however it had no statistically significant difference. It agreed with the study done by Sesso et al. (Sesso et al., 2004) who found 54% mortality in hospital admitted elderly patients with acute kidney failure.

Others found that AKI in hospital acquired had higher mortality(75%) than community acquired settings (46.9%) as declared by a study done in a group of hospitals in Tiwan over 4 years where they compare between CA.AKI and HA.AKI and the latter had higher levels of in-hospital mortality (26.07% vs 51.58%) (Chien-
Ning et al., 2016).

Bucuvic et al. (Bucuvic et al., 2011) studied short term mortality in a retrospective cohort with AKI from acute tubular necrosis, among them 65% were elderly. The reported mortality was 66% of patients. ICU admission and age older than 60 years were significant predictors of mortality.

The higher percentage of mortality in Bucuvic et al. study than the current research attributed to the selection of AKI from acute tubular necrosis in their study. As An intrinsic cause of AKI had worse outcomes when compared to pre-renal or postrenal causes of AKI (Yilmaz and Erdem, 2010).

The insignificant difference in mortality between CA.AKI and ICUA.AKI, was not the same in another

report (EL Bardai et al., 2015) although the latter group had worse SOFA score, older age group, and higher septic shock and hypovolemia. This could not be clearly explained; however it may be related to the difference in the earlier detection and the onset of intervention in ICUA.AKI than CA.AKI.

Gaps in the comparison of current result with other literatures might be, in part, attributed to the scanty of data about elderly ICUA.AKI rather than HA.AKI in comparison with CA.AKI, which warrants further research.

CONCLUSIONS

The incidence of AKI was 22.4%, in the current study. Patients with AKI were older than those without AKI. Anemia followed by hypovolemia then septic shock and baseline RF on dialysis were the predominant risk factors in patients with AKI rather than those without, according to their frequency. Higher age, hypovolemia, septic shock and diuretic use were significantly higher in ICUA.AKI than CA.AKI as risk factors, with no significant difference in baseline comorbidities.

RECOMMENDATION

More studies are needed about AKI in elderly patients especially in the ICU.

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It is from my pleasure to submit an article titled “Incidence of Community- Acquired Versus Intensive care unit Acquired Acute Kidney Injury in Two Tertiary intensive care units in aged patients" as Original paper to your journal. The content of this paper has not been published or submitted for publication elsewhere and approved by all co-authors. The protocol for the research project has been approved by Local Ethics Committee of hospitals within which the work was undertaken and that it conforms to the provisions of the Declaration of Helsinki. All subjects gave informed consent and patients’ anonymity were reserved. All authors have contributed significantly and are in agreement with the content of the manuscript

Conflict of Interest

The authors declare that they have no conflict of interest.

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