Etiology of acute kidney injury in intensive care unit settings

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Abstract

Introduction: Acute kidney injury (AKI) is defined as a rapid loss of kidney function occurring over few hours or days. In intensive care unit settings, acute kidney injury (AKI) is a very prevalent condition as most of the patients who are admitted in intensive care units are critically ill. The incidence of acute kidney injury is increasing throughout the world mainly because of aging population and comorbidities which are associated with aging. In intensive care unit settings, the incidence of AKI may reach up to 67%. Though AKI effects depend on clinical situation yet associated with high morbidity and mortality.

Objective: To determine the frequency of etiology of acute kidney injury in medical intensive care unit of KRL Hospital.

Setting: Medical ICU, KRL Hospital, Islamabad.

Duration: six months from 17th May 2017 to 17th November 2017.

Study design: Descriptive case series.

Material and method: In this study 118 patients were observed. After screening and application of exclusion criteria, a total of 118 patients who were fulfilling the inclusion criteria were selected as the study sample and were included in the final analysis regarding prevalence of risk factors associated with AKI. AKI was further classified using acute kidney injury network (AKIN) classification system. Patient age, gender, serum creatinine, etiology and outcome in form of recovery or mortality was recorded on specific proforma.

Results: Overall incidence of AKI in ICU settings in this study was 37.8%(n=118) .Out of 118 patients who had AKI, 59.3%(n=70) were male , whereas 40.7% (n=48) were females. Most common risk factor associated with development of AKI was sepsis secondary to infectious illnesses and 39% (n=46) of the patients who developed AKI were suffering from infectious illnesses. Gastrointestinal, drugs and cardiac causes constitutes the 32.2% (n=38), 18.6% (n=22) and 10.2% (n=12) respectively of the AKI in ICU settings.

Conclusion: Our study concludes that the frequency of etiology including infectious causes was 39%, cardiac pathology 10%, GI causes 32%, drugs was 19%

Key Words: etiology; infectious causes; cardiac pathology; GI causes; drugs; acute kidney injury

Introduction

Acute kidney injury (AKI) is defined as a rapid or abrupt loss of kidney function occurring over few hours or days [1]. The hallmark of acute kidney injury is raised serum creatinine levels and a raised blood urea nitrogen (BUN) concentration [2]. The clinical features of acute kidney injury (AKI) are very variable and there may be decrease in urine output or qualitative differences in urine solute concentrations in the absence of oliguria. In 50-60% of the patients diagnosed as having acute kidney injury (AKI), there is no decrease in urine output. Presence or absence of oliguria is related to prognosis of acute kidney injury (AKI). Complications of Acute kidney injury (AKI) include increase potassium level, metabolic acidosis, body fluid imbalance, uremia and patient may require dialysis.

Acute kidney injury (AKI) is an important health disorder affecting people throughout the world. It is considered as an important risk factor associated with development of complications and poor prognosis in hospitalized patients. Estimates from literature, regarding prevalence of acute kidney injury showed that 2000-3000 of per million population per

year is the incidence of less severe AKI. For severe AKI requiring dialysis, this incidence is 200-300 per million population per year.

Acute kidney injury (AKI) is mainly divided into three main categories which are pre-renal, intrinsic and post-renal AKI. The etiology of acute kidney injury is multifactorial. Important risk factors which are associated with development of acute kidney injury include sepsis, drugs, gastrointestinal losses and cardiac causes. Anaphylaxis can also lead to acute kidney injury (AKI).

In studies which were conducted on Hospital acquired acute kidney injury(HAAKI),it was found that, acute tubular necrosis (ATN) and pre-renal cause were the most common form of HAAKI in both medical and surgical ICUs associated with high mortality and morbidity [3]. Drugs were found as the most common cause of AKI in admitted hospital medical patients, whose incidence was 39.2% [4].

In another study sepsis was found as the most common cause of AKI followed by gastroenteritis as the second most common cause of AKI. Surgical, cardiac and hepatic causes were also found as a major contributor towards acute kidney injury [5].

The rationale of this study is that, as acute kidney has many risk factors, this study will be helpful in identifying important risk factor for development of acute kidney injury in ICU settings, leading to its early detection.

Materials and methods

This Descriptive case series was done in Medical ICU, KRL Hospital, Islamabad. Duration of the study was six months from 17th May 2017 to 17th November 2017. Sample size was calculated as 116 patients with 95 % confidence of interval and 6% margin of error and 12.4% expected percentage of AKI stage 1 in patients admitted in ICU with digestive system disorders. However in this study, screening of all the 312 patients admitted in medical ICU during 6 months of the study period for development of AKI was done and all 118 patients who were fulfilling the inclusion criteria after application of exclusion criteria were included in the final analysis for risk factors prevalence associated with AKI.

Sampling technique used was Non probability consecutive sampling. Patients of both gender, who develop acute kidney injury during ICU stay for at least ≥ 48hrs with age ranging between 18 and 70 are included in study.

Patients having previous history of chronic kidney disease, Patients having history of obstructive uropathy. Metastatic diseases affecting patient's survival, AKI in pregnancy, Surgery related causes of AKI, Patients not willing to participate in the study are excluded.

Data collection procedure

After approval of hospital ethical committee, all the patients admitted in medical ICU of KRL Hospital, Islamabad during the study period were screened for the presence of AKI and complete history and examination was done by the resident doctor. After screening and application of exclusion criteria, a total of 118 patients who were fulfilling the inclusion criteria were selected as the study sample and were included in the final analysis regarding prevalence of risk factors associated with AKI. It was further classified using acute kidney injury network (AKIN) classification system. Patient age, gender, serum creatinine, etiology and outcome in form of recovery or mortality was recorded. Confounding factors as laboratory error were double checked with pathology department. Intake/output record will also be double checked with nursing staff.

Statistical analysis was done in SPSS version 19. Qualitative data like gender, etiology, stages of AKI and outcome were presented as frequencies and percentages. Quantitative data like duration of ICU stay and age were presented as means and standard deviations. Effect modifiers like age, gender, duration of ICU stay and stage of AKI were controlled by stratification. Post stratification chi-square test was applied. P value ≤0.05 was considered significant. Results were presented in forms of tables and bar charts.

Results

In this study, screening of all the 312 patients, 183 males (58.6%) and 129 females (41.4%) admitted in medical ICU during 6 months of the study period for development of AKI was done and all 118 patients who were fulfilling the inclusion criteria were included in the final analysis for risk factors prevalence associated with AKI.

Ages of the patients were between 18 and 70 years and mean age and standard deviation (SD) was calculated as 52.88±13.39 years. Gender distribution among 118 patients was analyzed as 70(59.3%) patients were male and 48(40.7%) patients were female. (Table-1).

Duration of ICU stay was among 118 patients was analyzed as 67(57%) patients had stayed at ICU for <7 days and 51(43%) patients had stayed for more than 7 days. Status of AKI among 118 patients was analyzed as stage 1, stage 2 and stage 3 AKI were 41.5% (n=49), 39.0% (n=46) and 19.5% (n=23) respectively. (Table no 2)

Results regarding etiology of AKI in our study showed that, most common risk factor associated with development of AKI was sepsis secondary to infectious illnesses. 39% (n=46) of the patients who developed AKI were suffering from infectious illnesses. Other type of infectious illnesses leading to AKI included liver abscess, acute pancreatitis and infection from bed sores. Gastrointestinal diseases were found as the 2nd most common cause of AKI and 32.2% (n=38) of the patients who had AKI developed it secondary to gastrointestinal causes including gastrointestinal losses, gastrointestinal bleeding and liver dysfunction. Among these most common gastrointestinal cause was acute gastroenteritis followed by gastrointestinal bleeding 18.6% (n=22) and 10.2% (n=12) of the AKI was secondary to drugs and cardiac causes respectively (Table 3).

Stratification of etiology and mortality with age, gender, duration of ICU stay and stage of AKI is given in tables

Table 1. Age & gender distribution (n=118)

Age	Frequency	Percentages
≤ 45 years	50	42%
> 45 years	68	58%
Male	70	59.3%
Female	48	40.7%

Mean age was 52.88 years with SD ± 13.399

Table 2. Duration of ICU stay & stages of AKI (n=118)

Duration of ICU stay	Frequency	Percentages
≤ 7 days	67	57%
>7 days	51	43%
Stage I	49	41.5%
Stage II	46	39%
Stage III	23	19.5%

*Mean duration of ICU stay was 6.89 with SD ± 3.297

Table 3. Etiology (n=118)

Etiology	Frequency	Percentages
Infectious Causes	46	39%
Cardiac pathology	12	10.2%
GI Causes	38	32.2%
Drugs	22	18.6%
Total	118	100%

Table 4. Stratification of etiology w.r.t age & gender distribution (n=118)

AGE	infectious causes	Cardiac pathology	GI Causes	Drugs	Total	* P value
≤ 45 years	19(16%)	5(4%)	15(13%)	11(9.3%)	50(42%)	0.8781
> 45 years	27(23%)	7(6%)	23(19%)	11(9.3%)	68(58%)	
Male	27(23%)	7(6%)	22(19%)	14(12%)	70(59%)	0.9752
Female	19(16%)	5(4%)	16(13%)	8(7%)	48(41%)	

* Chi square test was applied in which P value was 0.8781 for age & 0.9752 for gender

Table 5. Stratification of etiology w.r.t duration of ICU & stages of AKI (n=118)

Duration	Infectious causes	Cardiac pathology	GI Causes	Drugs	Total	* P value
≤ 7 days	26(22%)	7(6%)	22(19%)	12(10%)	67(57%)	0.9944
> 7 days	20(17%)	5(4%)	16(13%)	10(8%)	51(43%)	
Stage I	19(16%)	5(4%)	16(13%)	9(8%)	49(51%)	0.9996
Stage II	18(15%)	5(4%)	15(13%)	8(7%)	46(39%)	
Stage III	9(8%)	2(2%)	7(6%)	5(4%)	23(19%)	

* Chi square test was applied in which P value was 0.9944 for duration of ICU & 0.9996 for stages of AKI

Discussion

Acute kidney injury (AKI) is defined as a rapid loss of renal function occurring over few hours or days. Complications of acute renal impairment includes increase potassium level, metabolic acidosis, body fluid imbalance, uremia and patient may require dialysis. AKI is one of common and major complication, associated with poor prognosis in patients which are admitted in intensive care unit settings. Although incidence of AKI is increasing throughout the world, data regarding its prevalence and prognosis in intensive care unit (ICU) in low resource setups is very little.

This study was planned to find out the incidence of AKI in ICU settings and also to know about the frequency of risk factors which are associated with development of AKI. Screening of all the 312 patients admitted in medical ICU during 6 months of study duration was done regarding presence of inclusion criteria and all 118 patients who fulfilled the inclusion criteria after application of exclusion criteria were included in the study. These 118 patients were studied regarding etiology of AKI. Theresults of this study that overall incidence of AKI in medical ICU of KRLHospital Islamabad was 37.8% (n=118).Out of these 118 patients who developed AKI, frequency of stage 1, stage 2 and stage 3 AKI was 41.5% (n=49), 39.0% (n=46) and 19.5% (n=23) respectively.

Although this study showed a high incidence of AKI in ICU settings but it was lower than the incidence of AKI found in an ICU study from Democratic Republic of Congo conducted in 2015, which showed an AKI incidence of 52.7% in ICU settings [1]. A review article suggested an overall all incidence of AKI in ICU settings ranging between 20-50%[6]
.However a study from Sri Lanka showed an even higher incidence of AKI in ICU settings, which was 60.2% [5]. The difference in prevalence of AKI is attributed to the different geographical distribution of risk factors leading to AKI and also due to usage of different diagnostic criteria and classification systems regarding evaluation of AKI.

In children, acute post streptococcal glomerulonephritis and hemolytic uremic syndrome are leading causes of intrinsic acute renal impairment. Studies have shown that AKI was present in 13.4% of those pediatric trauma patients who had post traumatic rhambdomyolysis[8]. A creatinine kinase level of ≥3,000 was found as an independent risk factor associatedwith development of AKI [8].

A long duration of extracorporeal cardiopulmonary bypass is commonly considered as risk factor associated with development of AKI. However according to one study duration of extracorporeal cardiopulmonary bypass does not predict development of AKI requiring dialysis, which shows that risk assessment can be a more reliable marker [9].

A study was conducted in Sri Lanka in 2014 to know about the frequencyof AKI in ICU settings & its etiology. According to results of this study 60.2% of the patients developed AKI during ICU admission. In this study, cardiac pathologies was found as the most common risk factor associated with development of AKI and results showed that 87% of the patients who had some cardiac pathology developed AKI during ICU stay. Sepsis wasfound as the 2nd leading cause of AKI and 63.5% of the patients who hadsepsis also had AKI [7].

A study was conducted in South India from May 2011 to October 2012 to know about prevalence of AKI in ICU settings including hospital acquired acute kidney injury (HAAKI) and the Community acquired acute kidney injury (CAAKI) and the risk factors associated with it. Thisstudy showed that about 25% of the patients had HAAKI while rest 75%were suffering from CAAKI [5].

In this study, a total of 500 patient were enrolled. The most common risk factor found to be associated with development of AKI in this study was sepsis. It was found that in 38.6% of the patients, cause of AKI was sepsis. Sepsis was most common secondary to urinary tract infection. Respiratory tract infections and diabetic foot infections were also major cause of sepsis in this study [5].

Gastroenteritis was found as the 2nd most common risk factor associated with development of AKI in this study. About in 10.4% of the patients, cause of AKI was gastroenteritis [5]. The third most common risk factor associated with development of AKI was obstetric disorders and about 8.4% of the patients with obstetric diseases developed AKI [5]. Surgical, hepatic and cardiac causes were also found as major contributor to the development of AKI in this study. Other diseases which were found to beassociated with development of AKI in this study included malaria, dengue, leptospirosis, drug induced AKI, snake bite, H1N1 influenza, multiple myeloma and rapidly progressive glomerulonephritis (RPGN). Out of 500 cases of AKI, in only 3 patients cause of AKI was hair dye poisoning and only 2 cases of AKI were reported to be associated with organophosphate poisoning [5].

A study was conducted in Kinshasa, the Democratic Republic of Congo in 2015 regarding incidence of AKI in ICU settings. In this study most common risk factors found to be associated with AKI was sepsis , whose incidence was 58.4%, 46.8% and 55.7% for stage 1,2 and 3 AKI according to acute kidney network classification (AKIN), followed by patients having disorder of circulatory system which was 42.5%, 37.7% and 42.6% respectively [1]. In this study a small number of patients developed AKI secondary to usage of nephrotoxic drugs like NSAIDs and some herbal medicines [1]. Some other studies from Sub Saharan Africa also showed infectious illnesses as the most common cause leading to development of AKI and it is likely due to large burden of malaria, sepsis, diarrheal disease, humanimmunodeficiency and virus (HIV) in this region [9].

Some other studies also identified circulatory failure, liver failure, hypovolemia, pulmonary disorders and infectious illnesses as main causes leading to AKI. Other risk factors associated with development of AKI include old age, hypertension, use of nephrotoxic drugs like NSAIDs and pre -existing kidney disease [10-12].

According to some studies, the most common etiology leading to intrinsic renal AKI in ICU settings is acute tubular necrosis (ATN), which is thought to be causing 88% of all the AKI cases in ICU settings [13-14]. However some studies suggested that, there is involvement of multiple etiologies in development of AKI in ICU settings [14].

Contrast enhanced imaging studies were also identified as a risk factor for development of AKI in various studies. Data suggested that over all incidence of acute renal impairment secondary to contrast enhanced studies is 11.5 % to 19 % [15-17]. Increased base line serum creatinine concentration, increased age, use of diuretics and other nephrotoxic drugs, use of vasopressors and reduction in mean arterial pressures are all thought related to increase in contrast enhanced renal injury [15-17].

In 2002, a large study was conducted in Austria, which involved 17000 patient from ICU settings including medical, surgical and mixed ICUs. Out of these 50.4% admissions were secondary to medical illnesses. It was found that 4.9% of the all patients admitted in ICUs were requiring dialysis. For medical ICU admission 5.6% of the patients were requiringdialysis while for surgical ICU 4.5% of the patients were given renal replacement therapy [18].The most important etiologies which were identified as a cause leading to renal replacement therapy in

this study included respiratory disease, sepsis, abdominal surgery, cardiovascular surgery, and other general surgical procedures [18].

Studies from surgical patients showed that prevalence of AKI was between 16.7% and 30% among the postoperative patients [19-20]. In a study, it was found that 70% of the patients post heart transplant developed AKI [21]. A study showed that, 54% of the patients who underwent surgical repair for acute aortic dissection developed AKI subsequently. It was found that 75% of these patients suffered from moderate hypothermia during the surgery but hypothermia alone was not found to be associated with increased risk of AKI in patients who underwent surgery of thoracic aorta [22].

Regarding etiology, the most common risk factor leading to AKI in this study was sepsis secondary to infectious causes and 39% (n=46)of the patients who developed AKI were suffering from infectious illnesses as the primary disease. This finding was consistent with many previous studies including a study from India conducted in 2014, which showed that most common cause of AKI was sepsis, accounting for 38,6% of thepatients [5]. Also a recent study from Democratic Republic of Congo suggested infectious illnesses as a leading cause of AKI [1].

In this study, gastrointestinal diseases accounted for the 2nd most commoncause leading to AKI and it included both gastrointestinal bleeding and gastrointestinal losses related illnesses and 32.2%(n=38) of the AKI patients had a gastrointestinal illness as the primary diagnosis. This resultwas similar to the result of study conducted in India, which also showed the gastroenteritis as the 2nd leading cause of AKI [5].However some other studies showed a lower incidence of gastrointestinal causes in AKIpatients [1].

In our study, drugs was also found as a risk factor significantly associatedwith development of AKI and 18.6% (n=22) of the AKI developed secondary to the side effects of nephrotoxic drugs. This finding is supported by some previous studies which showed that nephrotoxic drugslead to AKI in 19–25% of cases in the ICU [23-24].

Only 10.2% (n=12)of the AKI in our ICU was secondary to renal hypo perfusion caused by cardiac contractility dysfunction which was suggested by severe left ventricular systolic dysfunction on echocardiography in these patients. This incidence of AKI secondary to cardiac dysfunction was higher than study results from India, in which cardiac causes constitutes 6.8% of the AKI in ICU settings [2] but it was lower as compared to study conducted in Democratic Republic of Congo (DRC) [1]. These differences are attributed to the differences in geographical distribution of diseases and health care facilities.

In this study, higher stages of AKI were associated with longer ICU stay duration and it showed that AKI is associated with increased hospital stay and health care expenditure .This result is consistent with the previous studies which showed mean increase in ICU stay duration in patients withAKI as compared to those without AKI [5].

Although this study provided valuable information regarding etiology and prognosis of AKI in ICU settings, it has various limitations as well. Firstof all long term follow up was not done in the patients. Also base line creatinine before admission was not available in some cases and we had to use base line creatinine at admission in those cases. In our study group, many patients had comorbidities like diabetes, hypertension, chronic obstructive air way disease, ischemic heart disease and cerebrovascular diseases.

Conclusion

Our study concludes that the frequency of etiology including infectious causes was 39%, cardiac pathology 10%, GI causes 32%, drugs was 19%in patients with acute kidney injury.

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