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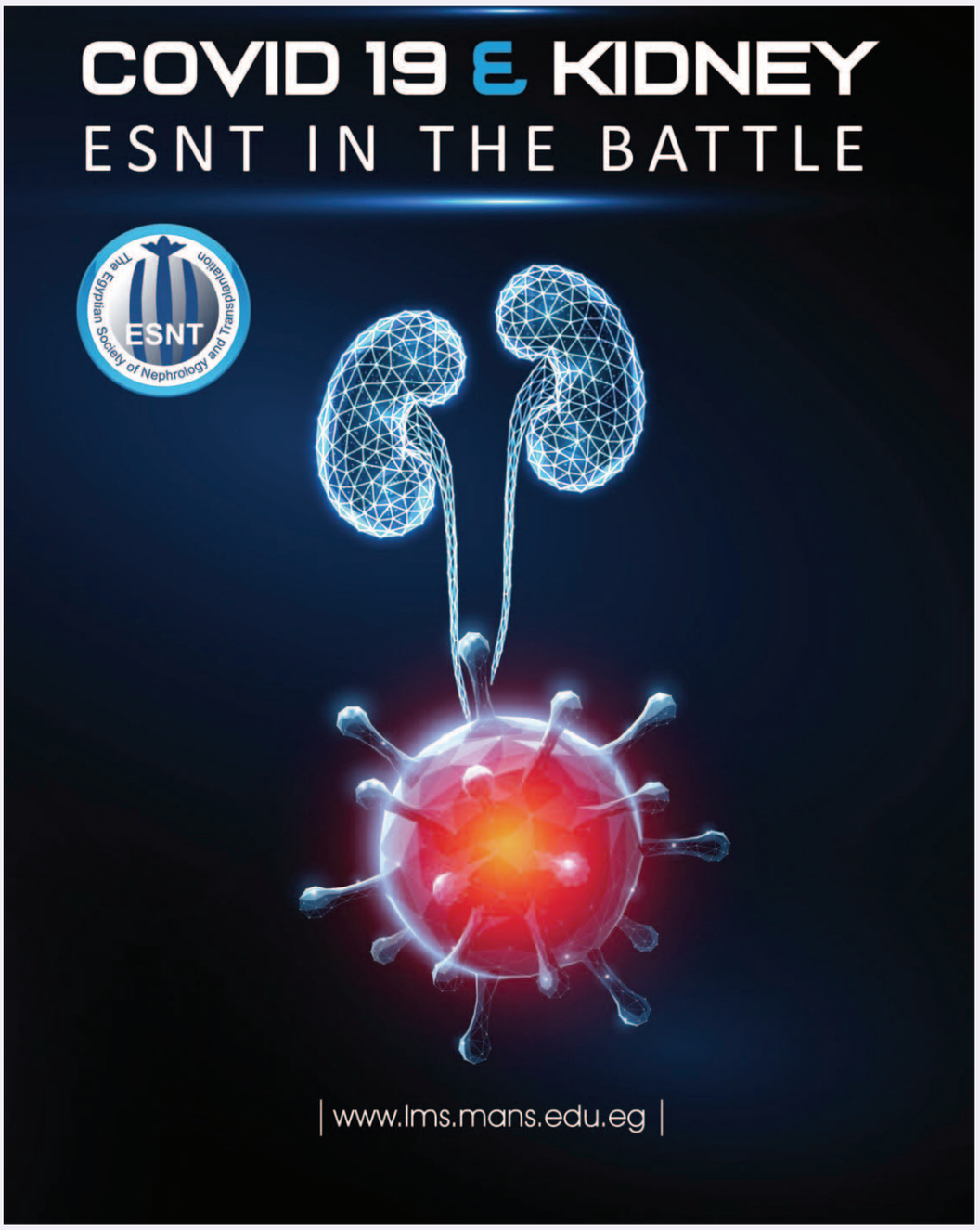

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Acute kidney injury in intensive care unit patients in Benha University Hospitals

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Background
Acute kidney injury (AKI) is classically described as abrupt or rapidly reversible reduction of excretion of nitrogenous waste products including urea, nitrogen, and creatinine. In critical care setting, patients with AKI constitute an important subgroup in that they have higher short-term and long-term mortality, prolonged hospital stay, and more resource consumption. Risk factors for AKI in patients with severe illness are multifactorial, including underlying certain predisposing factors, as aged patients tend to acquire AKI more than younger patients, together with underlying comorbidities AKI is common and carries a high mortality rate. Most epidemiological studies were retrospective and were done in Western populations.
Aim
The aim was to highlight the risk factors, mechanisms, and prognosis in AKI in patients in ICU.
Patients and methods
This is a prospective, observational study that was carried out in ICU, Benha University Hospitals, from January 2018 to July 2018. This study included 50 critical ill patients admitted to ICU. Oral and written consent was taken from every participant after explaining the procedures of the analysis. All patients were clinically evaluated and had routine assessment.
Results
The mean age of our studied population was 56.3±6.8 years, demonstrating a significant trend toward an increased number of AKI cases with older age. Males represented 68.9% of the included patients, and 62% of patients with AKI had a history of diabetes mellitus. Mortality was evident in 14% of patients with AKI. Patients with AKI with older age, male sex, diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, mechanical ventilation, and vasopressor were significantly associated with renal replacement therapy.
Conclusion
AKI was associated with high mortality rate, and early identification may cause a dramatic decrease in mortality and morbidity, which could be expected in these high-risk patients.

Keywords:
acute kidney injury, dialysis, intensive care units

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Introduction

Acute kidney injury (AKI) is a major global public health concern, with an incidence of ~2100 per million populations [1]. AKI development in ICU is associated with a risk of long-term renal dysfunction and short-term and long-term mortality [2].

AKI is characterized by a rapid deterioration of kidney function and accumulation of waste products, electrolytes, fluids, and also less obvious effects, including reduced immunity and dysfunction of nonrenal organs (organ cross-talk) [3].

The incidence of AKI is high and is increasing in patients admitted to ICU. Approximately 30–60% of critically ill patients have AKI based on RIFLE criteria, and of them, 4–5% require dialysis.

Underlying comorbidities predisposing to AKI include diabetes mellitus, hypertension, chronic kidney disease, and heart failure, all set the background for subsequent renal injury through the interplay of renal autoregulation, pre-existing renal damage, and concomitant use of nephrotoxic drugs.

Ischemia, inflammation, and direct toxic injury to the kidney are all major areas that contribute to the pathogenesis of AKI in critically ill patients.

Critically ill patients receive a myriad of medications including nephrotoxic drugs and antibiotics, which are responsible for 19–20% of AKI cases in ICU. Comorbidities that enhance the nephrotoxicity of the drugs are CKD, liver cirrhosis, and acute and chronic heart failure. Sepsis has been found to be the leading cause of AKI in ICU patients, and no single pathway can explain all features of septic AKI.

The current study aimed to highlight the risk factors, mechanisms, and prognosis in AKI in patients in ICU.

Patients and methods

Ethical approval was obtained from the Medical Institution Commission (27/8/2017), and a knowledgeable written informed consent with a proof concerning the concept of the analysis was taken from all of the registered patients. This is a prospective, observational study that was carried out in Benha University Hospitals at ICU from January 2018 to July 2018. This study included 50 critical ill patients admitted to ICU.

Inclusion criteria included age more than 18 years and patients who stayed in the ICU for longer than 48 h. Exclusion criteria included ICU admission of less than 48 h, postelective surgery, and ICU readmission. All included patients underwent detailed history taking, with special attention to age, residence, comorbid diseases such as diabetes, hypertension, and heart failure. Cause of admission, duration of hospital stay, risk factors of AKI, and nephrotoxic drugs were assessed. The patients were clinically evaluated generally, with stress on blood pressure respiratory rate, cardiac, chest, and abdominal examination, and laboratory investigations, which were done including complete blood picture, C-reactive protein, urine analysis, serum electrolyte (Na, K, Ca, and phosphorus), arterial blood gases, cardiac enzymes, serum creatinine, blood urea, chest radiography, and echocardiography.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using SPSS 19.0 for windows (SPSS Inc., Chicago, Illinois, USA). Data were expressed as mean ±SD. Analysis of variance test was used to assess the difference between the studied parameters in the studied groups. The frequencies were expressed in percentage. χ^2-Test was used to assess the difference between the studied frequencies in the studied groups. *P* was considered significant if less than 0.05 and highly significant if less than 0.001.

Table 1 Baseline data of the study population

	N (%)
Age (years)	
Mean±SD	56.3±6.8
25–44	3 (6)
45–64	41 (82)
≥65	6 (12)
Sex	
Male	34 (68)
Female	16 (32)
Diabetes mellitus	31 (62)
Sepsis	23 (46)
Congestive heart failure	
Hypertension	25 (50)
Cardiovascular disease	30 (60)
Chronic liver disease	
Hepatorenal disease	15 (30)
Nonhepatorenal disease	9 (18)
Chronic kidney disease	24 (48)
Cancer	28 (56)
GCS	13±2
Mortality	
Nonsurvivors	7 (14)
Survivors	43 (86)

GCS, Glasgow coma scale.

Table 2 Laboratory investigations of the study population

Creatinine (mg/dl) (mean±SD)	3.6±0.9
Urea (mg/dl)	143.4±44.4

Results

Analysis of the baseline data of the study population revealed that the mean age of our study population is 56.3±6.8 years, 68% of them are males, 62% of them are diabetics, 42% are hypertensive, 42% of them had history of cardiovascular diseases, 50% had chronic liver disease, 48% had chronic renal failure, and 56% of them had cancer. Mortality was evident in 14% of our study population (Table 1).

Analysis of laboratory investigations of our study population revealed that the mean of serum creatinine was 3.6±0.9 mg/dl, and the mean of serum urea was 143.4±44.4 mg/dl (Tables 2–4).

Comparison between patients with AKI who underwent renal replacement therapy (RRT) and patients with AKI without RRT regarding different parameters revealed, that there was no significant difference regarding Glasgow coma scale. Patients with AKI with RRT were older age than those without RRT. Males, diabetes mellitus (DM), chronic obstructive pulmonary disease, congestive heart failure, mechanical ventilation, vasopressor,

Table 3 Comparison between types of acute kidney injury regarding baseline data

	Pre renal (*N*=45) [*n* (%)]	Renal (*N*=5) [*n* (%)]	Tests	*P* value
Age (years)	60.2±8.1	57.3±7.8	*t*-test=2.9	0.449
Sex				
Male	31 (68.9)	3 (60)	χ^2=0.2	0.686
Female	14 (31.1)	2 (40)		
Diabetes mellitus	27 (60)	4 (80)	χ^2=0.8	0.382
Hypertension	23 (51.1)	2 (40)	χ^2=0.2	0.637
Heart Failure	27 (60%)	3 (60%)	χ^2=0	1
Chronic liver disease	21 (46.7)	3 (60)	χ^2=0.3	0.571
Chronic Kidney Disease	26 (57.8)	2 (40)	χ^2=0.6	0.447
Cancer	24 (53.3)	2 (40)	χ^2=0.3	0.571
Cause	Sepsis: 23 (46)	Vascular: 2 (4)		
	Hypovolemia: 2 (4)	Intrinsic: 3 (6%)		
	Heart failure: 5 (10)			
	Hepatorenal syndrome: 15 (30)			

Table 4 Comparison between types of acute kidney injury regarding laboratory investigations

	Prerenal (*N*=40)	Renal (*N*=5)	*t* test	*P* value
Creatinine (mg/dl)	3.6±0.7	3.5±0.9	0.3	0.769
Urea (mg/dl)	144.2±51.1	147.3±49.1	0.1	0.897

Table 5 Comparison between acute kidney injury regarding treatment

	AKI with RRT (*N*=14) [*n* (%)]	AKI without RRT (*N*=36) [*n* (%)]	Tests	*P* value
Age (years)	62.3±7.8	53.4±5.5	*t*-test=4.6	0.000
Sex				
Male	4 (28.6)	28 (77.8)	χ^2=10.6	0.001
Female	10 (71.4)	8 (22.2)		
Diabetes mellitus	13 (92.9)	18 (50)	χ^2=7.9	0.005
COPD	12 (85.7)	4 (11.1)	χ^2=25.8	0.000
Congestive heart failure	11 (78.6)	3 (8.3)	χ^2=24.7	0.000
Mechanical ventilation	8 (57.1)	3 (8.3)	χ^2=14	0.002
Vasopressors	9 (64.3)	3 (8.3)	χ^2=17.3	0.000
GCS	14.2±4.3	13.6±2.2	*t*-test=0.7	0.517

AKI, acute kidney injury; COPD, chronic obstructive pulmonary disease; GCS, Glasgow coma scale; RRT, renal replacement therapy.

and Acute Physiology and Chronic health Evaluation II (APACHE-II) and Sequential Organ Failure Assessment (SOFA) scores were significantly increased among RRT group (Tables 5 and 6).

Comparison between survivors and nonsurvivors regarding baseline data revealed that there was no significant difference between the two groups regarding age, sex, DM, hypertension, congestive heart failure, chronic liver disease, chronic kidney disease, and cancer (Table 7 and Figs. 1–3).

Comparison between survivors and nonsurvivors regarding laboratory investigations revealed that nonsurvivors had significant increased values of serum creatinine, whereas there was no significant difference between the two groups regarding serum urea (Figs. 4 and 5).

Discussion

In the present study, 94% of the studied patients were aged more than 45 years. Old age is a well-defined risk factor of occurrence of AKI and related to compromised kidney function owing to aging-induced physiological and pharmacokinetic changes. Moreover, elderly patients have comorbid conditions for which they are using medications, including nephrotoxic drugs, which make them more susceptible to AKI [4].

In the present study, males represented 68.9% of the included patients. Previously, it was demonstrated that the rate of AKI development was the same in either sex [5]. In accordance with our findings, Malleshappa *et al.* [6] found that male represented 62.3% of ICU patients with AKI. Doddakula *et al.* [7] identified that female patients with AKI were associated with a higher risk of dialysis requirement.

In the current study, 62% of patients with AKI had a history of DM. These findings are in accordance with the findings of Schmitz *et al.* [8], as they noted that critically ill patients with diabetes have a higher incidence of developing AKI. This can be explained as hyperglycemia induces release of free fat acids, the inactivation of nitric oxide (NO), and increased

Table 6 Multivariate regression analysis to determine risk factors for mortality in acute kidney injury

	Coefficients	SE	*t* statistics	*P* value	Lower 95%	Upper 95%	Lower 95.0%	Upper 95.0%
DM	0.163	0.108	1.51	0.138	−0.054	0.381	−0.054	0.381
HTN	0.016	0.103	0.161	0.872	−0.193	0.226	−0.193	0.226
CVD	−0.169	0.107	−1.571	0.123	−0.386	0.048	−0.386	0.048
CLD	−0.050	0.103	−0.490	0.626	−0.259	0.158	−0.259	0.158
CRF	−0.081	0.109	−0.748	0.458	−0.302	0.138	−0.302	0.138
Cancer	0.009	0.107	0.088	0.929	−0.208	0.227	−0.208	0.227

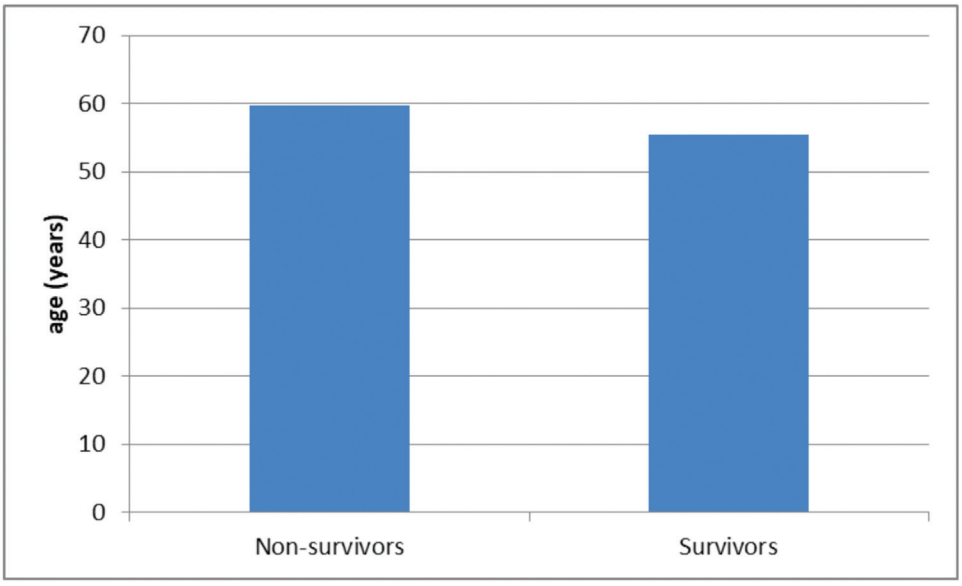
CLD, chronic liver disease; CRF, chronic renal failure; CVD, cardiovascular disease; DM, diabetes mellitus; HTN, hypertension.

Table 7 Comparison between survivors and nonsurvivors regarding baseline data and laboratory investigation

	Nonsurvivors (*N*=8) [*n* (%)]	Survivors (*N*=42) [*n* (%)]	*t* test	*P* value
Age (years)	59.7±5.8	55.5±7.2	1.4	0.181
Sex				
Male	4 (66.7)	27 (69.2)	0.016	0.904
Female	2 (33.3)	12 (30.8)		
Diabetes mellitus	5 (83.3)	23 (60)	1.3	0.251
Hypertension	2 (33.3)	15 (38.5)	0.06	0.809
Heart Failure	2 (33.3)	21 (53.8)	0.9	0.349
Chronic liver disease	2 (33.3)	19 (48.7)	0.5	0.481
Chronic kidney disease	3 (50)	22 (56.4)	0.1	0.768
Cancer	3 (50)	21 (53.8)	0.03	0.861
Creatinine (mg/dl)	4.6±1.2	3.4±0.8	3.2	0.002*
Urea (mg/dl)	139.5±46.6	144.5±45.2	0.3	0.802

*Significant difference $P<0.05$.

Figure 1



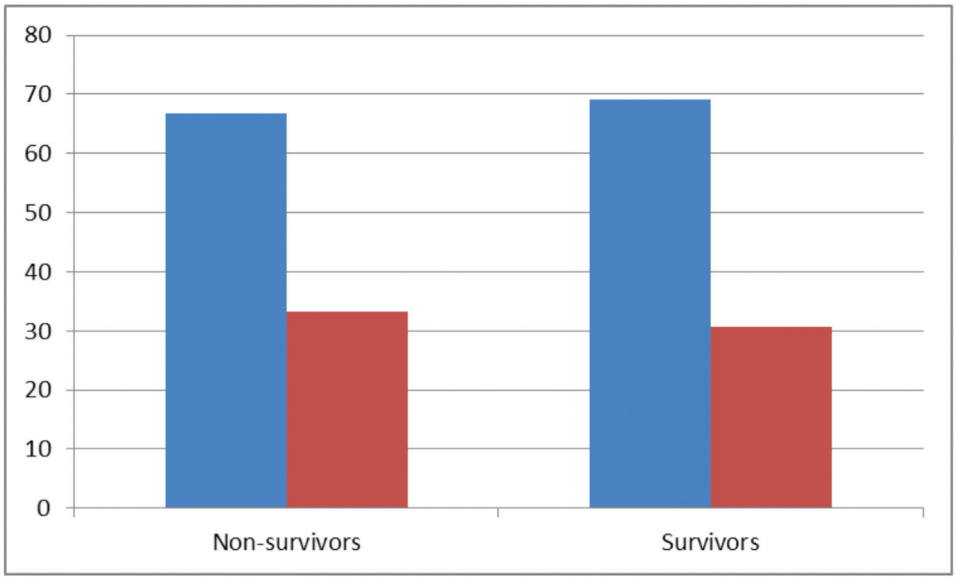
Comparison between survivors and nonsurvivors regarding age.

production of reactive oxygen species (ROS), correspondingly [9].

However, Nisula *et al*. [10], found no significant difference between patients with AKI and those without AKI regarding history of DM as DM was evident in 22% of ICU patients with AKI.

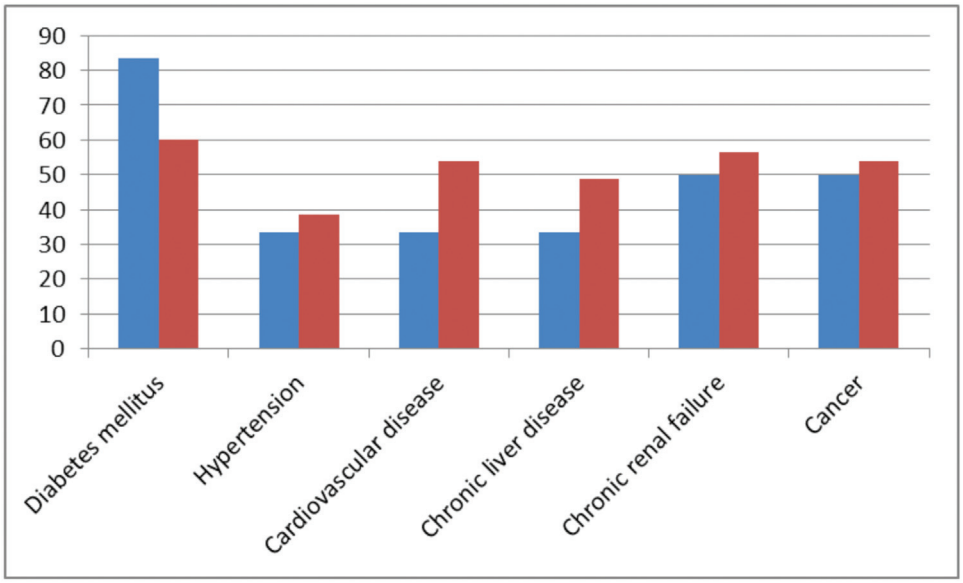
In the current study, 53% of patients with AKI have cancer. This can be explained as patients with cancer are particularly at risk for AKI secondary to infection and sepsis [11], tumor lysis syndrome [12], kidney damage induced by immunosuppression after hematopoietic stem cell transplantation [13], and direct effects from the primary malignancy [14].

Figure 2



Comparison between survivors and nonsurvivors regarding sex.

Figure 3



Comparison between survivors and nonsurvivors regarding morbidity.

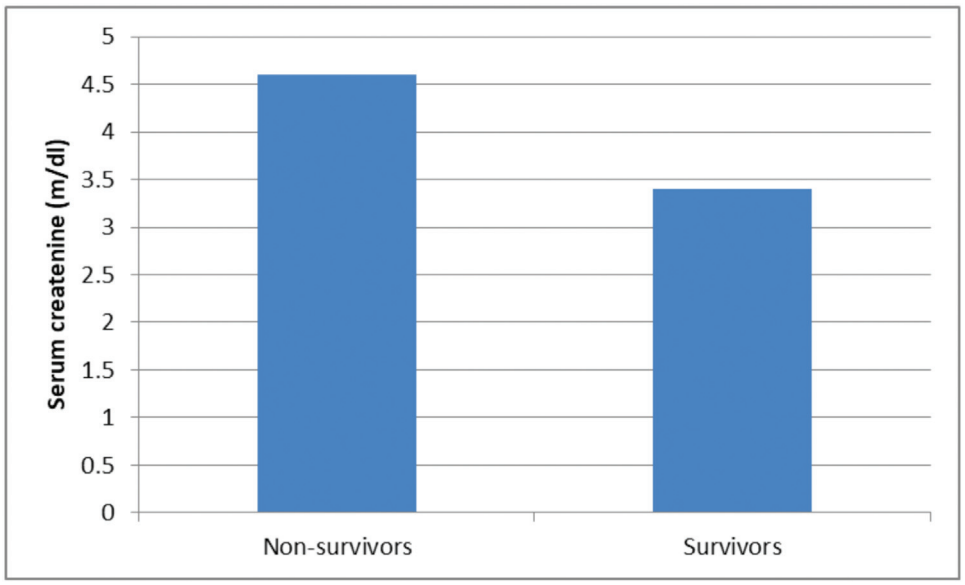
However, these findings disagree with the findings of Mao and Qin [15], as they noted no significant difference between patients with AKI and those without AKI regarding history of malignancy as cancer was evident in 25.5% of ICU patients with AKI.

AKI in ICU is multifactorial, and true etiology is still needed to be evaluated [16]. Primary diagnosis on ICU admission may vary from clinicians to clinicians; therefore suggest studies with well-defined diagnostic criteria are suggested in order to determine the exact cause of AKI [15].

In the present study, congestive heart failure was evident in 60% of patients with AKI. It was reported that heart failure is often regarded as one of the most important risk factors for perioperative AKI [17].

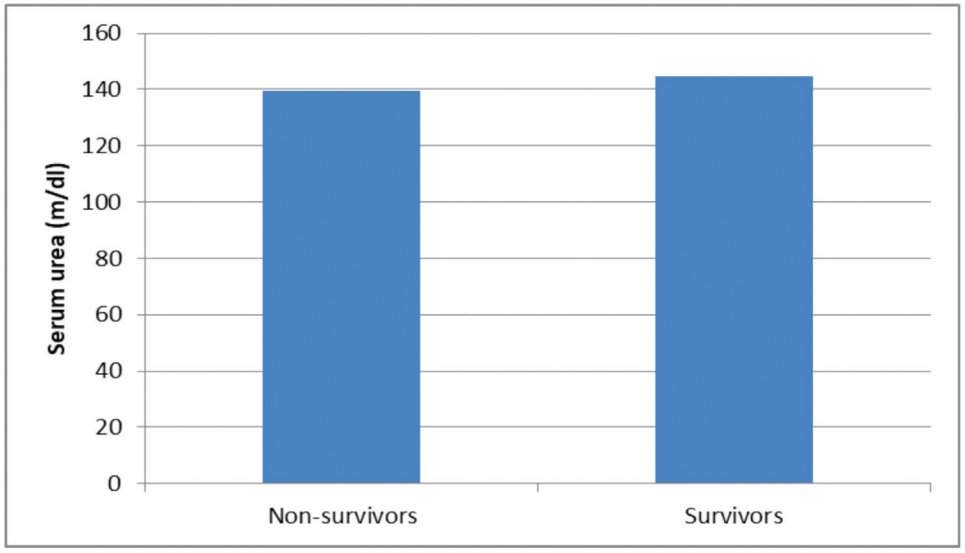
In the present study, chronic liver disease was evident among 30% of the included patients. Piano and his colleagues [18] reported that AKI has an estimated prevalence of ~20–50% among hospitalized patients with cirrhosis and patients with cirrhosis are more likely to develop renal failure compared with individuals without liver disease.

Figure 4



Comparison between survivors and nonsurvivors regarding serum creatinine.

Figure 5



Comparison between survivors and nonsurvivors regarding serum urea.

In the present study, mortality was evident in 14% of the studied population. AKI is independently associated with short-term and long-term mortality [2]. Critically ill patients with AKI are ~2–5 times more likely to die compared with those without AKI, with mortality exceeding 50% [19].

Patients with AKI in ICU are usually managed with conservative treatments or RRT. Conservative treatment includes management of volume, electrolyte, and acid-base homeostasis and specific drug management. RRT is indicated for management of specific problems such as volume overload, hyperkalemia, acidosis and symptoms of uremia [20].

Because of limited health resources and complications associated with RRT, many critically ill patients with AKI are often managed conservatively with mechanical ventilation, inotropes, diuretics, and intravenous fluids; RRT is usually initiated when major complications of fluid overload, acidosis, uremia, or hyperkalemia

develop. Early prediction of the requirement for acute RRT would be useful in ICU where physicians have excessive workload [15].

Therefore, several risk factors of dialysis treatment were determined in the current study. In this context, the current study determined risk factors of dialysis treatment among patients with AKI. Patients with AKI with old age were found to be significantly associated with dialysis treatment. Similar findings were reported by Elsevier *et al.* [20] that patients with AKI requiring RRT were significantly older than those who did not need RRT in ICU. We also identified that female patients were associated with a higher risk of dialysis requiring AKI and similar findings have been reported by Doddakula *et al.* [7].

In the present study, presence of congestive heart failure and chronic obstructive pulmonary disease was associated with dialysis. These results are in agreement with other findings evaluating different factors of RRT need among patients with AKI [7].

In this study, the dialysis treatment was significantly associated with DM. Faulk *et al.* [21] have also reported association of DM with RRT.In this study, the percentage of patients who were treated with vasopressor drugs was significantly increased among RRT group. Myc *et al.* [22] found that estimated glomerular filtration rates were also significantly lower in the AVP group.

In the present study, the percentage of patients who needed mechanical ventilation was significantly increased among RRT group. Doddakula *et al.* [7] found that ventilator duration and pulmonary complications are significantly associated with RRT risk.

Other risk factors of dialysis initiation were mechanical ventilation and high disease severity scores. The severity of disease, as evaluated by recognized prognostic scales in ICU, considerably affects the risk of dialysis treatment [23]. The results of the current study also showed increased risk of dialysis with high SOFA and APACHE-II results.

These results are also in concordance with the findings of Czempik *et al.* [24] where they found that dialysis increased with each score increase. Need of mechanical ventilation and vasopressors denotes seriously ill patients, as evidenced by the high Glasgow coma scale, APACHE-II, and SOFA scores, and these patients had higher risks of dialysis in the present study. These findings are consistent with other studies conducted in ICU [7].

Conclusion

AKI was associated with high mortality rate and. Early identification may cause a dramatic decrease in mortality and morbidity in these high-risk patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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