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Incidence, Clinical Characteristics and Outcome of Acute Kidney Injury among Critically Ill patients in Zagazig University Hospitals

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ABSTRACT

Background: There is marked variety in Acute Kidney Injury (AKI) incidence and clinical characteristics as regards independent developmental risk factors and independent risk factors that could affect the outcome especially in critical care setting.

Objectives: The aim of the work was to identify incidence and the clinical features of AKI in critical care situation and its impression on outcomes.

Patients and Methods: A prospective cohort study in which patients were screened for AKI during the period from October 2018 to September 2019 using the AKIN criteria.

Results: Incidence of AKI in critical care setting was 20.3% (63/310). The most independent risk factors for the development of AKI based on multivariate Logistic analysis were sepsis (p value: 0.000, estimated odds ratio: 4.492 and confidence intervals between 2.037 and 9.906) and chronic kidney disease (CKD) (p<0.001, estimated odds ratio: 8,982 and confidence intervals between 3,852 and 20,945). The most independent risk factor for poor AKI outcome was the need for renal replacement therapy (RRT) based on a multivariate logistic analysis (p<0.001, estimated odds Ratio: 3.649 and confidence interval between 1.145 and 4.050). Late nephrologist consultation comes in second place (p=0.002, estimated odds ratio: 4.902 and confidence interval between.463 and 9.316). Mortality in AKI group was 31% (3 patients in stage 2 and 17 patients in stage 3) compared to 42/247 (17%) in patients without AKI.

Conclusion: The incidence of AKI in Zagazig University Internal Medicine ICU was 20.3 %. Sepsis was the most independent risk factor for the occurrence of AKI in ICU. The most independent risk factors for poor outcome following AKI development were the need for RRT, Late nephrologist consultation, longer duration of AKI and a high APACHE score.

Keywords: Acute Kidney Injury, CKD, AKIN criteria, APACHE score, Outcome.

INTRODUCTION

Acute kidney injury is a common medical problem especially in critical care setting that has negative impact as regard patients outcome and health care resources. It has multiple risk factors and causes [(1)]. AKI has incidence ranges from 20 to 70 percent in critical care setting [(2)]. High rate of hospital mortality ranges between 50-70% occur in patients with AKI undergoing RRT and about 25-50% of patients develop chronic renal disease [(3)]. As a consequence, identification of the precipitating factors for occurrence of AKI among thosecategory of patients has great beneficial effect in reduction of the incidence of AKI among that category of patients [(2)].

Several risk factors for occurrence of AKI in critical care setting has been identified, these factors are more nuanced rather than being single risk. Elderly patients appear to experience AKI more often than younger patients due to physiological ageing of the kidneys, presence of co-morbidities and impaired renal capacity for recovery. [(4)]. Patients with history of diabetes mellitus (DM), hypertension or underlying chronic kidney disease , have high susceptibility for renal injury that could result from presence of renal damage from underlying co-morbidity, use of nephrotoxic drugs or defect in regenerating capacity of kidneys [(5)]. Interestingly, CKD is an important risk factor for occurrence of AKI, many patients with AKI develop CKD [(6)].

The aim of the work was to identify incidence and the clinical features of AKI in critical care situation and its impression on outcomes therefore we could improve the consequence of occurrence of AKI among that high-risk category of patients.

PATIENTS AND METHODS

This prospective cohort study included a total of 310 patients for potential occurrence of AKI, admitted to the

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Internal Medicine Intensive Care Units (ICUs), Zagazig University Hospitals. This study was conducted between October 2018 and September 2019. Written informed consent was obtained from all study participants after the explanation of the study objectives and nature and assuring that confidentiality will be maintained throughout the work.

***Ethical Consideration*:**

The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University, prior to the study (10/2018). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

After excluding patients with End-Stage Renal Disease (ESRD) on regular hemodialysis and patients who were admitted to ICU for duration of less than 48 h.

Patients were divided into two major groups according to the occurrence of AKI in group A (patients with AKI) and group B (patients without AKI) and then group A divided into three subgroups according to stage AKI according to the AKIN criteria into:

- **Stage 1:** Serum creatinine increase ≥26.5 μmol/l (≥0.3 mg/dl) OR increase to 1.5–2.0-fold from baseline or urine output <0.5 ml/kg/h for 6 h.
- **Stage 2:** Serum creatinine increase >2.0–3.0-folds from baseline or urine output <0.5 ml/kg/h for 12 h.
- **Stage 3:** Serum creatinine increase >3.0-folds from baseline OR serum creatinine ≥354 μmol/l (≥4.0 mg/dl) with an acute increase of at least 44 μmol/l (0.5 mg/dl) OR urine output <0.3 ml/kg/h for 24 h OR Anuria for 12 h OR need for RRT.

Patients were subjected to complete history taking, thorough clinical examination, and routine investigations including (complete blood picture, serum creatinine, urea, liver function tests, total and ionized calcium and serum phosphorus) and pelvi abdominal ultrasound with stress on both kidneys.

The risk factors that could affect the development of AKI include age, use of the following drugs (diuretics, NSAIDs, ACEI and ARBs), presence of sepsis, underlying disease (DM, HTN, HF and CKD), duration of AKI, time of nephrological consultation and use of renal replacement therapy.

Statistical analysis

All data were collected, tabulated and statistically analyzed using SPSS 24.0 for windows (SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. Chi square test (χ^2) and Fisher exact was used to calculate difference between qualitative variables as indicated. One-way ANOVA test was used to compare between more than two dependent groups of normally distributed variables. Pearson's and Spearman's correlation coefficient were used for correlating normal and non-parametric variables respectively. The (+) sign was considered as indication for direct correlation i.e. increase frequency of independent lead to increase frequency of dependent & (-) sign as indication for inverse correlation i.e. increase frequency of independent lead to decrease frequency of dependent, also we consider values near to 1 as strong correlation & values near 0 as weak correlation. Multiple regression analysis was performed where logistic regression coefficients (B) are calculated and used to estimate odds ratios (EXP(B)) for different independent factors as predictors of acute renal injury (AKI) diagnosis among patients admitted to cardiac and medical intensive care. All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates Non-significant difference.

RESULTS

The current study included 310 patients who were admitted to the Zagazig University Hospital Intensive Care Unit and monitored during their admission to ICU for potential occurrence of AKI and were divided into two major groups according to the occurrence of AKI in group A (patients with AKI) and group B (patients without AKI) and then group A was distributed into three subclasses according to stage of AKI according to the Acute Kidney Injury Network (stage 1, stage 2 and stage 3).

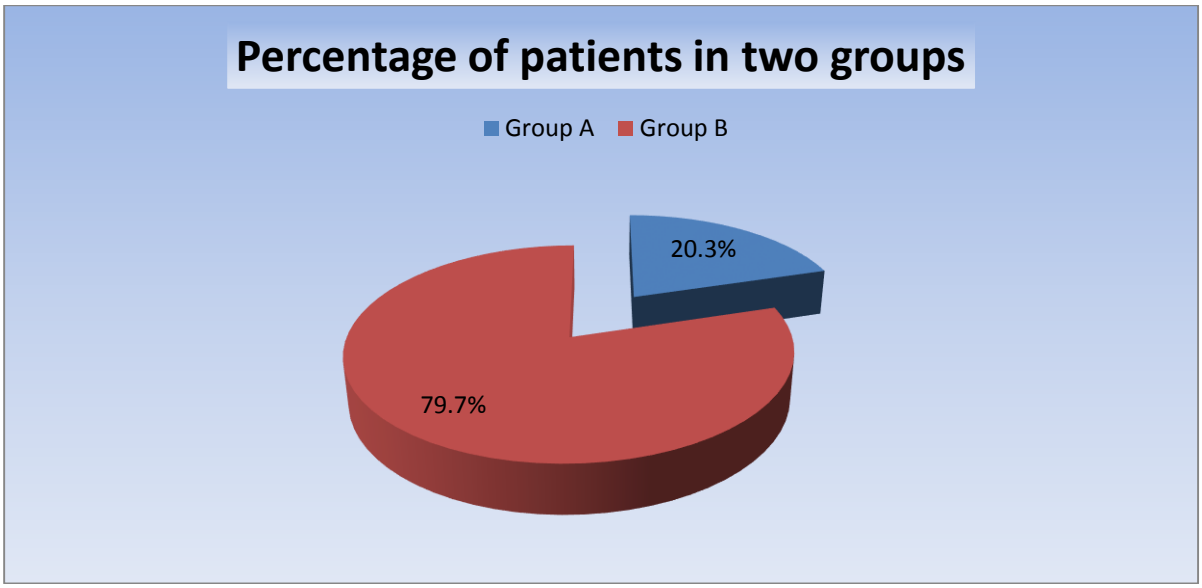

Figure (1): Pie chart showing Distribution of the studied population:

Demographic data:

We could not find statistical difference between (group A & group B) concering the mean of age (±SD) (group A 58.6±14.11& group B 57.5±14.19). However, we found statistical difference between (group A & group B) regarding gender (t=4,955) (p<0,05).

Table (1): Demographic distribution of the patients in the two main groups (group A & group B):

		Group A (AKI)	Group B (Non AKI)	T	P
Age (Years) Mean (±SD)		58.6±14.11	57.5±14.19	0.550	0.582
Gender	Male	21 (33.3%)	121 (49%)	4.955	0.026
	Female	42 (66.7%)	126 (51%)		

Assessment of Patients at Presentation

As regards the distribution of patient history (group A & group B), we found significant statistical differences in smoking prevalence (t=9.372) (p<0.05), HTN (t=11.7) (p<0.05), CKD (t=50.33) (p<0.05). As regards the mean (±SD) of the APACHE score, it was significantly higher in Group A compared to Group B (t=5.402) (p<0.05). Similarly, the prevalence of sepsis was significantly higher in Group A compared to Group B (t=28.58) (p<0.05).

Table (2): Distribution of medical history of patients in the two main groups (group A &group B):

	Group A (AKI) (N 63)	Group B (Non AKI) (N 247)	t	P
Smoking	5 (7.9%)	64 (25.9%)	9.372	0.002
Hypertension (HTN)	47(74.6%)	125 (50.6%)	11.7	0.001
Diabetes Mellitus (DM)	23(36.5%)	83 (33.6%)	0.188	0.664
Chronic kidney disease	29 (46%)	22(8.9%)	50.33	0.001

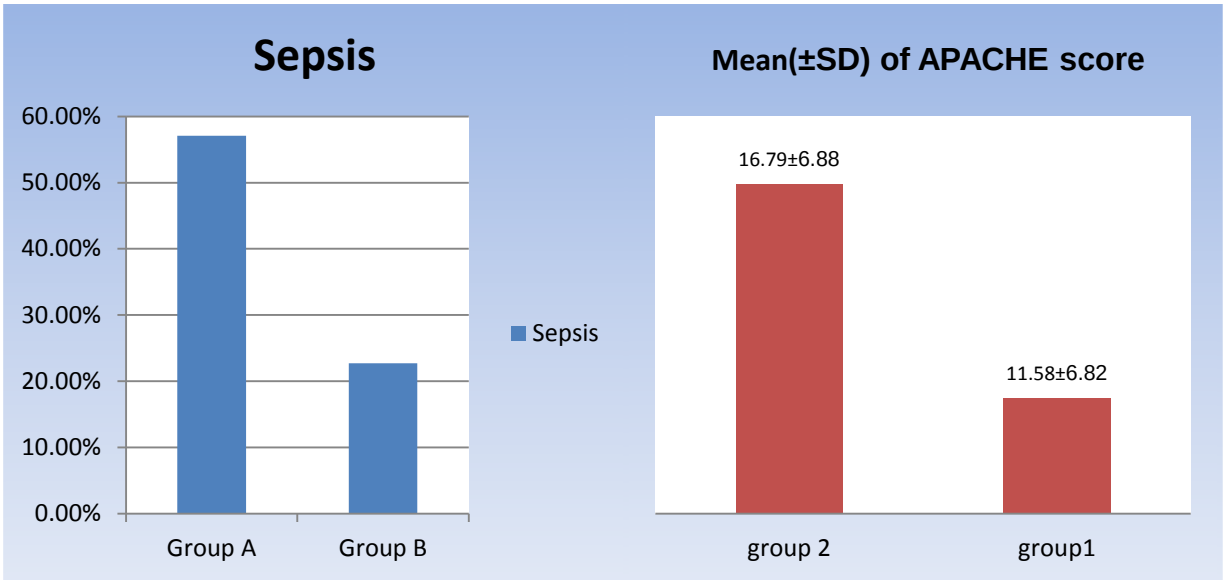

Figure (2): Simple bar chart showing comparison between the two main groups (group A & group B) as regards prevalence of sepsis and mean (±SD) of APACHE score:

Differences in outcome:

We found Significant difference between (Group A & Group B) as regards the outcome (t=50.33) (p<0.05).

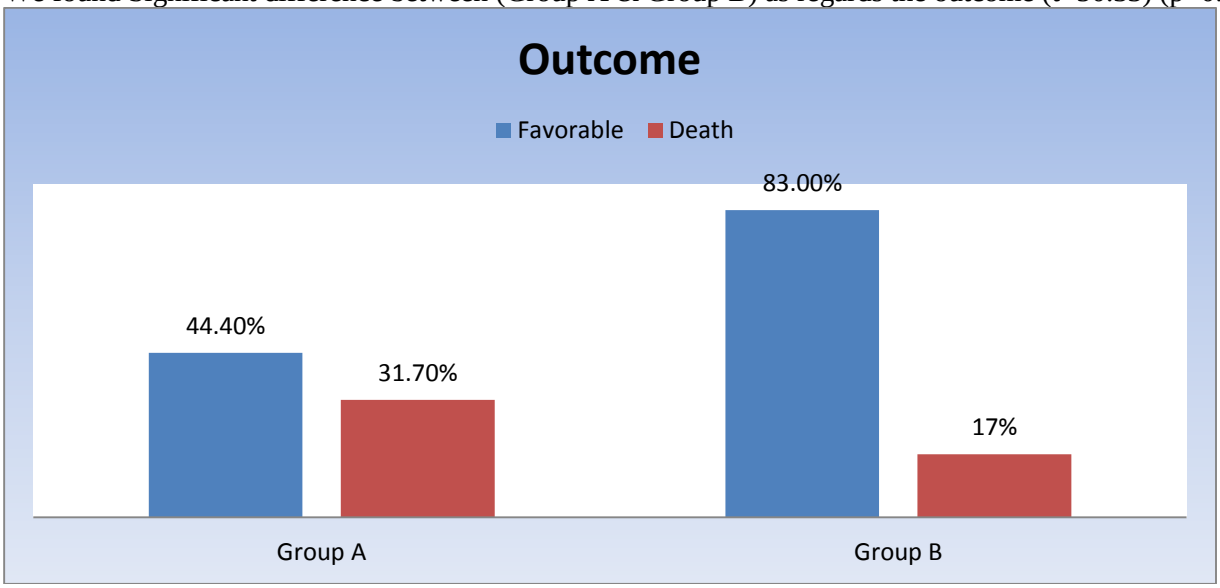

Figure (3): Simple bar chart showing comparison between the two main groups (group A &group B) as regards outcome:

As regards group A (AKI group):

Patients in this group were divided depending on stage of AKI to stage1, 2 and stage 3. Stage 1 (0 patients 0%), stage 2 (18 patients 28.5%) and stage 3 (45 patients 72.5%). No significant difference between the subgroups of group A as regards the mean age (±SD) of stage 2 (58.5±17.32) of stage 3 (58.64±12.82) or gender (t=0.350) (p=0.554). The prevalence of CKD was significantly higher in Stage 3 subgroup A (t=5.751) (P<0.05). As regards the mean (±SD) of the APACHE score and sepsis prevalence were significantly high in stage 3 subgroup of group A (t=2.69) (P<0.05) and (t=8.873) (P<0.05) were significantly higher. As regards the mean (±SD) of the maximum s.cr level and the prevalence of oliguria, they were significantly higher in stage 3 subgroup of group A (t=2.337) (P<0.05) and (t=9.961) (P<0.05) without significant differences in basal creatinine level (t=1.734) (P=0.09) respectively. As regards the mean duration (±SD) of AKI it was significantly higher in stage 3 subgroup of group A (t=2.654) (P<0.05) and the requirement for RRT, it was significantly higher in stage 3 subgroup of group A (t=3.977) (P<0.05).

Table (3): Demographic data, medical history, clinical data and laboratory differences between CKD and non-CKD patients among group A:

		CKD (N=29)	Non-CKD (N=34)	t / χ^2	P
Age(years) Mean ± SD		60.31 ± 13.64	57.15 ± 14.53	.886	.379
Sex	Male	5 (17.2%)	16 (47.1%)	6.262	.012
	Female	24 (82.8%)	18 (52.9%)		
APACHE (%) Mean ± SD		17.9 ± 6.51	15.85 ± 7.15	1.178	.243
Baseline creatinine Mean ± SD		2.86 ±0.732	0.927 ±0.222	6.893	.001
Max Creatinine Mean ± SD		7.32 ± 1.68	4.46 ± 1.79	3.505	.001
Consult Creatinine Mean ± SD		6.21 ± 1.72	3.51 ± 0.66	4.844	.001
Duration(weeks) Mean ± SD		4.62 ± 0.68	2.41 ± 0.23	2.929	.005
Oliguria		23 (79.3%)	14 (41.2%)	9.39	.002
RRT		20 (69%)	10 (29.4%)	9.817	.002
DM		17 (58.6%)	6 (17.6%)	11.335	.001
HTN		26 (89.7%)	21 (61.8%)	6.426	.011

Table (4): Difference between variables according to outcome in AKI patients.

		Favorable (N=28)	CKD stage 5D (N=15)	Death (N=20)	F/ χ^2	P
Age(years) Mean ± SD		58.71 ± 14.52	59.53 ±14.38	57.75 ±13.99	.068	.934
Sex	Male	10 (35.7%)	4 (26.6%)	7 (35%)	.396	.820
	Female	18 (64.3%)	11 (73.3%)	13 (65%)		
APACHE (%) Mean ± SD		12.64 ± 5.86	17.33± 6.98	22.2 ± 3.69	17.215	.001
Baseline creatinine Mean ± SD		1.1 ± 0.489	2.97 ± 0.801	1.95 ± 0.14	25.79	.001
Max Creatinine Mean ± SD		3.64 ± 0.02	8.28 ± 2.44	6.89 ± 0.62	14.34	.001
Duration(weeks) Mean ± SD		1.93 ± 0.858	6.47 ± 1.87	3.35 ± 0.13	14.53	.001
Oliguria		5 (17.9%)	14 (93.3%)	18 (90%)	34.8	.001
Early consult		28 (100%)	7 (46.7%)	7 (35%)	25.7	.001
Late consult		0	8 (53.3%)	13 (65%)		
DM		8 (28.6%)	7 (46.7%)	8 (40%)	1.534	.464
HTN		20 (71.4%)	11 (73.3%)	16 (80%)	.469	.791
RRT		2 (7.1%)	12 (80 %)	16 (80%)	33.1	.000
Stage 2		14 (50%)	1 (7.7%)	3 (15%)	11.63	.003
Stage 3		4 (50%)	4 (93.3%)	7 (85%)		

We found that the most common cause of AKI was sepsis 35/63 (55.6 per cent) followed by dehydration 14/63 (22.2 per cent), cardio-renal 6/63 (9.5 per cent), drug induced 3/63 (4.8 per cent), lupus activity 2/63 (3.2 per cent), hypovolemic shock 2/63 (3.2 per cent) and rhabdomyolysis 1/63 (1.6 per cent).

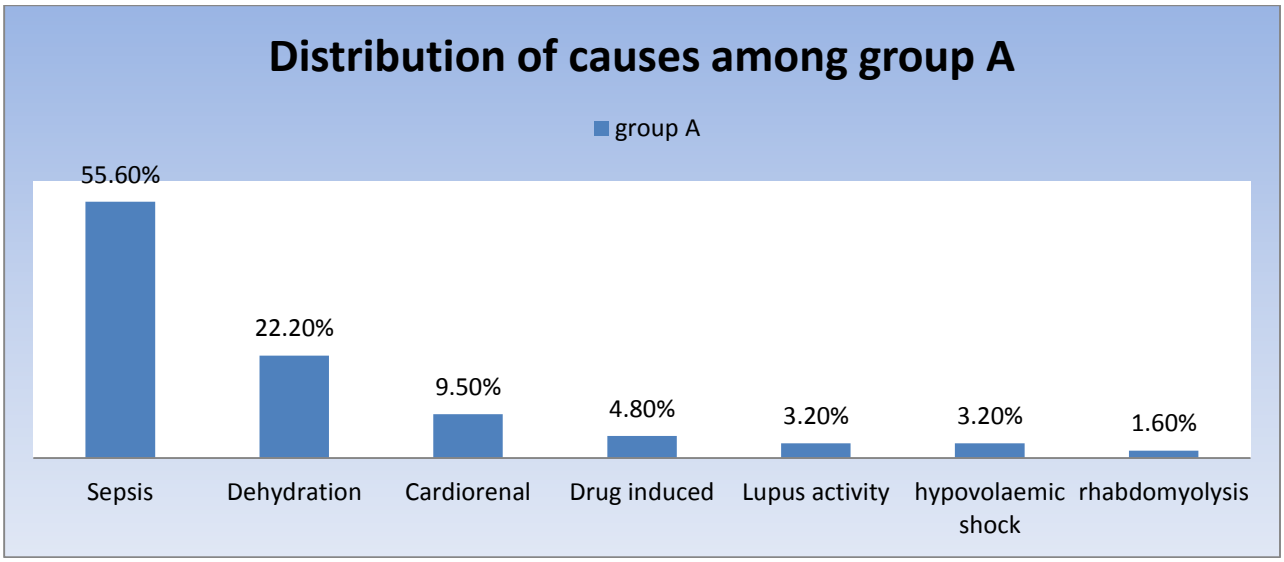

Figure (4): Simple bar chart showing distribution of causes of AKI among group A:

- Existence of Smoking, High APACHE score ≥19, Existence of Sepsis, Existence of DM and Existence of CKD were independent risk factors for the occurence of AKI.
- APACHE score ≥15, Raised levels of createnine after admission, Late consultation, Existence of sepsis, requirement for RRT and Longer period of AKI were independent predictors of poor outcome.

Table (5): Multivariate Logistic regression analysis to determine the risk factors for AKI:

Variable	OR	S.E.	Wald	Sig.	95% C.I.	
					Lower	Upper
Age	1.008	.013	.419	.517	.983	1.034
Female	1.052	.371	.019	.891	.509	2.177
Smoking	.160	.592	9.547	.002	.050	.512
APACHE	.942	.026	5.134	.023	.894	.992
Sepsis	4.492	.403	13.866	.000	2.037	9.906
DM	.381	.394	5.986	.014	.176	.825
HTN	1.890	.405	2.471	.116	.855	4.179
CKD	8.982	.432	25.825	.000	3.852	20.945

Table (6): Multivariate Logistic regression analysis to determine the factors predicting the outcome in in AKI patients.

Variable	OR	S.E.	Wald	Sig.	95% C.I.	
					Lower	Upper
Age	1.005	.045	.015	.904	.921	1.098
Female	.415	1.271	.479	.489	.034	5.011
APACHE	1.258	.102	5.078	.024	1.030	1.537
Baseline creatinine	11.796	1.423	3.008	.083	.725	191.815
Max creatinine	.671	.386	1.069	.031	.315	1.429
Late consult	4.902	.961	3.194	.002	.463	9.316.
DM	.982	1.158	.000	.987	.101	9.509
Sepsis	.344	0.528	4.096	.043	.122	.967
HTN	.730	1.733	.033	.856	.024	21.798
Duration	1.246	.187	2.728	.030	.886	1.847
RRT	3.649	.026	7.377	.000	.1.145	4.050
Stage 3	1.164	1.516	.010	.920	.060	22.725

DISCUSSION

Acute kidney injury considered to be a major clinical problem due to severe renal and systemic consequences, therefore it has been the focus of numerous nephrology studies [(7)]. In spite of marked improvement of care provided for those categories of patients, AKI incidence remain high among hospitalized individuals especially those category of patients receiving intensive care [(8)]. Mortality rate remaining as high as eighty percent of patients with AKI receiving intensive care and 13 percent of survivors require dialysis. These proportions persisted virtually unchanged despite the optimization of care [(9)] due to difficult and late diagnosis of AKI, advanced patient age, the presence of multiple comorbidities, and a higher number of invasive procedures in patients [(10)].

In the current study, among 310 patients admitted to our internal medicine intensive care unit, between October 2018 and September 2019, the incidence of AKI was 20.3 per cent. Similarly, **Abd El Hafeez *et al.*** [(11)] reported that incidence of AKI in critical care setting was (37.4%). Meanwhile, **Luo *et al.*** [(12)], **Levi *et al.*** [(13)], **Reddy *et al.*** [(14)] and **Reginaldo *et al.*** [(15)] reported **51%, 63%, 46%** and **40.5%** of AKI incidences in ICUs.

In the current study, we found that the presence of DM (P=0.014) and CKD (P=0.000) was an independent risk factor for AKI development in critical care setting. **Eswarappa *et al.*** [(16)] reported that the risk factors were sepsis (38.6%), diabetes mellitus (30.6%), hypertension (29.2%) and heart disease (11.4%). These results were comparable to those of **Levi *et al.*** [(13)] who found that the risk factors for AKI development were hypertension (65.8%), heart disease (46.8%), sepsis (42%) and diabetes mellitus (33%).

We found that APACHE II score > 19 was an independent risk factor for the occurrence of AKI (P=0.023) and APACHE II score > 15 was a predictor for poor outcomes among patient experienced AKI in critical care setting (P=0.024). **Samimagham *et al.*** [(17)] also found that high APACHE II scores were an independent risk factor for increasing mortality rate. In the case of **Peres *et al.*** [(18)], there was increase risk of AKI among patients with high APACHE II scores on admission.In the current study, sepsis was the most important independent risk factor for the occurrence of AKI (P=0.000) and an independent predictor poor outcome (P=0.043) among patients experienced AKI in critical care setting. Similarly, **Nashwa *et al.*** [(19)] reported that sepsis was the most serious risk factor for occurrence of AKI in critical care setting (p=0,001). Similarly, **Abd El Hafeez *et al.*** [(11)] found that sepsis was the most important independent factor for the occurrence of AKI in critical care setting.

In our study, we found that presence of oliguria had major negative impacts on long term as regards mortality (P=0.000) and development of stage 5 D CKD (P=0.000), similar to **Federspiel *et al.*** [(20)] who reported that urine output < 0.5 ml / kg / h was related to poorer outcome as regards recovery of renal function. **Peres *et al.*** [(18)] on the other hand, pronounced oliguria as an independent risk factor for mortality.

In the current study, we found that late nephrologist consultation was an independent predictor of poor outcomes among patients experienced AKI in critical care setting (P=0.002). Similarly, **Costa *et al.*** [(21)] reported that delayed nephrology consultations were related to higher mortality and increased dialysis dependence among patient experienced AKI in critical care setting. Similarly, **Débora *et al.*** [(22)] found that delayed intervention of nephrologist contribute to higher AKI mortality.

In the current study, we found that the longer duration (> 7 days) of AKI was an independent predictor of poor outcomes (P=0.030) among patients experienced AKI in critical care setting. Similarly, **Han *et al.*** [(7)], found that the longer the duration of AKI, the higher the mortality rate, the longer the hospital stays and the higher the rate of development of ESRD than the patients with short duration of AKI. The strong correlation between duration of AKI and poor outcome can be explained as follows: the more severe and treatment-resistant the case of AKI (e.g. non-recovery), the longer the duration of AKI becomes. Similarly, **Mehta *et al.*** [(23)] found that the longer the duration of AKI, the higher possibility of development of cardiovascular events, with long-term mortality and higher rate for the development of a CKD.

In the current study, we found that patients with stage 3 AKI (AKIN criteria) was associated with a higher mortality rate and a higher risk of non-recovery of renal function (P=0.003). Similarly, **Chang et al** [(24)] found that mortality rate was progressive and significant on the basis of the AKIN criteria. Similarly, **Truche *et al.*** [(25)] found that the rate of renal recovery was significantly different between the AKI stages (65.62%, 62.74% and 45.60% for the AKI stages 1, 2 and 3 respectively).

In the current study, we found that the number of patients receiving RRT was 30 (47.6%) with significantly higher RRT levels among patients with history CKD (69% vs. 29.4% among non-CKD patients). Need for RRT was an independent predictor of poor outcomes (P=0.000) among patients experienced AKI in intensive care setting. Similarly, **De Corte *et al.*** [(26)] who found that the rate of major renal adverse events among patients experienced AKI in critical care setting receiving RRT was 87.5%. This result is very consistent with **Meersch *et al.*** [(27)] which found that there was an increase in the

rate of major adverse renal events among patients experienced AKI in critical care setting treated with RRT after 1 year of treatment.

CONCLUSION

Acute kidney injury is a common clinical situation with serious complications especially in critical care setting with long term and short term negative consequences as regards morbidity and mortality. Sepsis was the main risk factor for AKI development in intensive care setting. Several risk factors associated with occurrence and poor consequences in patients with AKI but our study found that APACHE score ≥15, elevated creatinine levels after admission, Late consultation, Presence of Sepsis, need for RRT and Longer duration of AKI were independent predictor of poor outcomes.

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Conflicts of Interest: The authors declare no conflict of interest.

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